http://bit.ly/2Xidfid

Scientists uncover a trove of genes that could hold key to how humans evolved

Dozens of genes previously thought to have similar roles across species are in fact unique to humans

Researchers at the Donnelly Centre in Toronto have found that dozens of genes, previously thought to have similar roles across different organisms, are in fact unique to humans and could help explain how our species came to exist.

These genes code for a class of proteins known as transcription factors, or TFs, which control gene activity. TFs recognize specific snippets of the DNA code called motifs, and use them as landing sites to bind the DNA and turn genes on or off.

Previous research had suggested that TFs which look similar across different organisms also bind similar motifs, even in species as diverse as fruit flies and humans. But a new study from Professor Timothy Hughes' lab, at the Donnelly Centre for Cellular and Biomolecular Research, shows that this is not always the case.

Writing in the journal Nature Genetics, the researchers describe a new computational method which allowed them to more accurately predict motif sequences each TF binds in many different species. The findings reveal that some sub-classes of TFs are much more functionally diverse than previously thought.

"Even between closely related species there's a non-negligible portion of TFs that are likely to bind new sequences," says Sam Lambert, former graduate student in Hughes' lab who did most of the work on the paper and has since moved to the University of Cambridge for a postdoctoral stint. "This means they are likely to have novel functions by regulating different genes, which may be important for species differences," he says.

Even between chimps and humans, whose genomes are 99 per cent identical, there are dozens of TFs which recognize diverse motifs between the two species in a way that would affect expression of hundreds of different genes.

"We think these molecular differences could be driving some of the differences between chimps and humans," says Lambert, who won the Jennifer Dorrington Graduate Research Award for outstanding doctoral research at U of T's Faculty of Medicine.

To reanalyze motif sequences, Lambert developed new software which looks for structural similarities between the TFs' DNA binding regions that relate to their ability to bind the same or different DNA motifs. If two TFs, from different species, have a similar composition of amino-acids, building blocks of proteins, they probably bind similar motifs. But unlike older methods, which compare these regions as a whole, Lambert's automatically assigns greater value to those amino-acids-- a fraction of the entire region-- which directly contact the DNA. In this case, two TFs may look similar overall, but if they differ in the position of these key amino-acids, they are more likely to bind different motifs. When Lambert compared all TFs across different species and matched to all available motif sequence data, he found that many human TFs recognize different sequences--and therefore regulate different genes-- than versions of the same proteins in other animals.

The finding contradicts earlier research, which stated that almost all of human and fruit fly TFs bind the same motif sequences, and is a call for caution to scientists hoping to draw insights about human TFs by only studying their counterparts in simpler organisms.

"There is this idea that has persevered, which is that the TFs bind almost identical motifs between humans and fruit flies," says Hughes, who is also a professor in U of T's Department of Molecular Genetics and Fellow of the Canadian Institute for Advanced Research. "And while there are many examples where these proteins are functionally conserved, this is by no means to the extent that has been accepted."

As for TFs that have unique human roles, these belong to the rapidly evolving class of so-called C2H2 zinc finger TFs, named for zinc ion-containing finger-like protrusions, with which they bind the DNA.

Their role remains an open question but it is known that organisms with more diverse TFs also have more cell types, which can come together in novel ways to build more complicated bodies.

Hughes is excited about a tantalizing possibility that some of these zinc finger TFs could be responsible for the unique features of human physiology and anatomy--our immune system and the brain, which are the most complex among animals.

Another concerns sexual dimorphism: countless visible, and often less obvious, differences between sexes that guide mate selection--decisions that have an immediate impact on reproductive success, and can also have profound impact on physiology in the long term. The peacock's tail or facial hair in men are classic examples of such features.

"Almost nobody in human genetics studies the molecular basis of sexual dimorphism, yet these are features that all human beings see in each other and that we are all fascinated with," says Hughes. "I'm tempted to spend the last half of my career working on this, if I can figure out how to do it!"

The research was funded by grants from the Canadian Institutes of Health Research, the National Science and Engineering Research Council, and the US National Institutes of Health. Hughes also holds the Billes Chair of Medical Research at the University of Toronto.

http://bit.ly/2EGj2qu

Whales: gigantism and cancer suppression evolved concurrently

Humpback genome adds to growing understanding of 'Peto's Paradox'.

Andrew Masterson reports.

As whales evolved to become gigantic, the genetic changes needed to accomplish the feat were accompanied by others that drastically reduced the primary danger of growing huge: cancer.

That's the conclusion reached by a team of researchers led by Marc Tollis of the Biodesign Institute at Arizona State University in the US and published in the journal *Molecular Biology and Evolution*.

In some respects, the risk of cell mutations that develop into cancer is a brute numbers game, broadly conditional on the number of cells in any given organism, not merely at any given moment, but across lifespan.

Large whales, such as the blue (*Balaenoptera musculus*) and the humpback (*Megaptera novaeangliae*), have around 1000-times more cells than a human and can live for 90 years or more. On the figures, therefore, they should be particularly susceptible to cancer.

However, as far as scientists have been able to determine, they are not. Indeed, all gigantic mammals – elephants, for instance – appear to have lower rates of cancer than their cell counts should suggest.

This situation, acknowledged for years, is known as Peto's Paradox, named after a researcher who in 1975 showed that an increase in cancer occurrences in mammals as they age was due to the cumulative effects of lifetime dose and not any intrinsic effect of ageing.

A humpback whale: huge, heavy and (relatively) cancer-free. **MIGUEL MEDINA/AFP/Getty Images**

In the latest research, Tollis and colleagues constructed – for the first time – the complete genome of a humpback whale, and then compared it to existing genomes for 10 other species.

The results confirmed earlier research that found that gigantism is linked to the duplication of many genes that are associated with cell function, DNA repair and ageing.

Bowhead whales *(Balaena mysticetus*), for instance, have been estimated to live for at least 200 years, and their genome shows positive selection of a gene called ERCC1, which is an important component of the DNA repair pathway. The species also has duplications in other genes that influence gene repair and cellular growth.

Similar duplications were found in the genomes of other species.

“Altogether, these results suggest that the genomes of larger and longer-lived mammals may hold the key to multiple mechanisms for suppressing cancer, and as the largest animals on Earth, whales make very promising sources of insight for cancer suppression research,” the researchers write.

https://bbc.in/2EDUiiB

Fertility paradox in male beauty quest

Scientists have uncovered an evolutionary paradox where men damage their ability to have children during efforts to make themselves look more attractive.

By James Gallagher Health and science correspondent, BBC News

Taking steroids to get a buff physique or anti-baldness pills to keep a full head of hair can damage fertility. It has been named the Mossman-Pacey paradox after the scientists who first described it.

They say it causes a lot of heartache in couples struggling to conceive.

"I noticed some men coming in to have their fertility tested and these guys were huge," says Dr James Mossman, now at Brown University in the United States. He was studying for his doctorate in Sheffield when he made the connection with steroid abuse.

He told the BBC: "They are trying to look really big, to look like the pinnacles of evolution. "But they are making themselves very unfit in an evolutionary sense, because without exception they had no sperm in their ejaculation at all."

Anabolic steroids mimic the effect of the male hormone testosterone in the body and are used as performance-enhancing drugs to increase muscle growth. They are regularly used by bodybuilders.

Prof Allan Pacey, from the University of Sheffield, added: "Isn't it ironic that men go to the gym to look wonderful, for the most part to attract women, and inadvertently decrease their fertility."

Anabolic steroids fool the brain's pituitary gland into thinking the testes are going into overdrive. So the glands react by shutting down the production of two hormones - called FSH and LH - which are the key hormones that drive the production of sperm.

The researchers say there is a similar theme in men using medication to prevent male pattern baldness. The drug finasteride changes the way testosterone is metabolised in the body and can limit hair loss, but side effects can include erectile dysfunction and a hit to fertility.

Prof Pacey told the BBC: "I would say more anabolic steroid users are likely to become sterile than you would think - 90% probably.

"Baldness is a bit more hit-and-miss, but sales are going through the roof and that makes it an increasingly common problem."

'Evolutionary dud'

The measure of success in evolutionary terms is passing on your genes (instructions in your DNA) to the next generation. Dr Mossman said taking these vanity-based medications might make you more attractive but could turn you into "an evolutionary dud".

It is not the equivalent of the extravagant peacock's tail, which makes males more attractive to females and increases the chances of passing genes on to the next generation.

There are some examples in the natural world where an animal sacrifices their ability to breed. Some bird species perform co-

operative breeding in which individuals forego having their own offspring to help raise the descendants of close relatives.

But even this can make sense in evolutionary terms as half of your genes are shared with siblings so they are still being passed on, just indirectly. Dr Mossman suspects "thinking you're more appealing to the opposite sex, but killing your fertility" is probably unique to humans.

Prof Pacey told the BBC: "The irony is one thing, but I think the key message is for fertility patients. "It keeps cropping up in clinics and the message is not getting out to young men that it's a problem and a bit of info could save them a lot of heartache."

http://bit.ly/2I80O26

Scientists zoom in on bug behind strep throat and scarlet fever

Nearer to developing a vaccine that could one day could prevent hundred of thousands of infections annually

LONDON - Scientists studying a bacterium that causes scarlet fever, severe sore throat and a form of heart disease say they are closer to developing a vaccine that could one day prevent hundred of thousands of infections a year.

In a study in the journal Nature Genetics, scientists from Britain and Australia found detailed differences between strains of Group A Streptococcus bacteria — known as Strep A — from 22 countries, but also found several molecular targets common across many strains, offering potential for vaccine development.

Strep A is one of the world's top 10 causes of death from infectious diseases. It is estimated to cause more than half a million deaths every year.

It can cause several different infections, ranging from strep throat to scarlet fever, which are constant threats in many parts of the world, to an illness called rheumatic heart disease, which can affect certain populations including Aboriginal Australians.

There is no effective vaccine for Strep A, and efforts to develop one have been hampered by the huge number and variety of Strep A strains — meaning it is very tricky to develop a vaccine that could be effective against all of them.

In this work, researchers from Britain's Wellcome Sanger Institute and Cambridge University, and from Australia's Doherty Institute and Queensland University, sequenced the DNA of more than 2,000 Strep A samples from 22 countries, including in Africa and from Australian Aboriginal communities.

"Using all the data we collected, we narrowed down common genes in almost all strains of Strep A globally," said Mark Davies of the Wellcome Sanger and Doherty institutes, who co-led the work.

"This is a tremendous step forward in identifying what may work as a global vaccine candidate."

Mark Walker, director of the Australian Infectious Diseases Research Centre, said the findings should "renew the momentum" and enable a fast-track approach to a global Strep A shot since potential drug developers could use the database to find the molecular targets most likely to lead to an effective vaccine.

http://bit.ly/2EF9sDZ

Music helps to build the brains of very premature babies

Researchers from UNIGE and HUG demonstrate how music specially composed for premature infants strengthens the development of their brain networks and could limit the neurodevelopmental delays that often affect these children

In Switzerland, as in most industrialized countries, nearly 1% of children are born "very prematurely", i.e. before the 32nd week of pregnancy, which represents about 800 children yearly. While advances in neonatal medicine now give them a good chance of survival, these children are however at high risk of developing neuropsychological disorders. To help the brains of these fragile

newborns develop as well as possible despite the stressful environment of intensive care, researchers at the University of Geneva (UNIGE) and the University Hospitals of Geneva (HUG), Switzerland, propose an original solution: music written especially for them. And the first results, published in the Proceedings of the National Academy of Sciences (PNAS) in the United States, are surprising: medical imaging reveals that the neural networks of premature infants who have listened to this music, and in particular a network involved in many sensory and cognitive functions, are developing much better.

***Premature baby listening to music.* © Stéphane Sizonenko - UNIGE HUG**

The Neonatal Intensive Care Unit at the HUG welcomes each year 80 children born far too early - between 24 and 32 weeks of pregnancy, i.e. almost four months ahead of schedule for some of them. The vast majority will survive, but half will later develop neurodevelopmental disorders, including learning difficulties, attentional or emotional disorders. "At birth, these babies' brains are still immature. Brain development must therefore continue in the intensive care unit, in an incubator, under very different conditions than if they were still in their mother's womb," explains Petra Hüppi, professor at the UNIGE Faculty of Medicine and Head of the HUG Development and Growth Division, who directed this work. "Brain immaturity, combined with a disturbing sensory environment, explains why neural networks do not develop normally."

A tailor-made music

The Geneva researchers started from a practical idea: since the neural deficits of premature babies are due, at least in part, to unexpected and stressful stimuli as well as to a lack of stimuli adapted to their condition, their environment should be enriched by introducing pleasant and structuring stimuli. As the hearing system is functional early on, music appeared to be a good candidate. But which music? "Luckily, we met the composer Andreas Vollenweider, who had already conducted musical projects with fragile populations and who showed great interest in creating music suitable for premature children," says Petra Hüppi.

Lara Lordier, PhD in neurosciences and researcher at the HUG and UNIGE, unfolds the musical creation process. "It was important that these musical stimuli were related to the baby's condition. We wanted to structure the day with pleasant stimuli at appropriate times: a music to accompany their awakening, a music to accompany their falling asleep, and a music to interact during the awakening phases." To choose instruments suitable for these very young patients, Andreas Vollenweider played many kinds of instruments to the babies, in the presence of a nurse specialized in developmental support care. "The instrument that generated the most reactions was the Indian snake charmers' flute (the punji)," recalls Lara Lordier. "Very agitated children calmed down almost instantly, their attention was drawn to the music!" The composer thus wrote three sound environments of eight minutes each, with punji, harp and bells pieces.

More efficient brain functional connections through music

The study was conducted in a double-blind study, with a group of premature infants who listened to the music, a control group of premature infants, and a control group of full-term newborns to assess whether the brain development of premature infants who had listened to the music would be more similar to that of full-term babies. Scientists used functional MRI at rest on all three groups of hildren. Without music, premature babies generally had poorer functional connectivity between brain areas than full-term babies, confirming the negative effect of prematurity. "The most affected

network is the salience network which detects information and evaluates its relevance at a specific time, and then makes the link with the other brain networks that must act. This network is essential, both for learning and performing cognitive tasks as well as in social relationships or emotional management," says Lara Lordier.

In intensive care, children are overwhelmed by stimuli unrelated to their condition: doors open and close, alarms are triggered, etc. Unlike a full-term baby who, in utero, adjusts its rhythm to that of its mother, the premature baby in intensive care can hardly develop the link between the meaning of a stimulus in a specific context. On the other hand, the neural networks of children who heard Andreas Vollenweider's music were significantly improved: the functional connectivity between the salience network and auditory, sensorimotor, frontal, thalamus and precuneus networks, was indeed increased, resulting in brain networks organisation more similar to that of full-term infants.

When children grow up

The first children enrolled in the project are now 6 years old, at which age cognitive problems begin to be detectable. Scientists will now meet again their young patients to conduct a full cognitive and socio-emotional assessment and observe whether the positive outcomes measured in their first weeks of life have been sustained.

This study is financed by the Swiss National Science Foundation as well as, among others, by the Prim'Enfance Foundation.

http://bit.ly/2I92q42

Researchers find 28% of 35- to 50-year-old men studied are at-risk for osteoporosis

Loss of bone mineral density occurring at younger ages in both genders, according to study in the Journal of the American Osteopathic Association

CHICAGO - Research published in The Journal of the American Osteopathic Association found 28 percent of men and 26 percent of women between 35 and 50 years of age had osteopenia, a precursor to osteoporosis.

The findings surprised the participants and researchers, who did not expect the condition to be more prevalent in men. Osteopenia occurs when bones are weaker than normal, but do not yet break easily.

The research suggests bone health assessments can help middle-aged adults understand their future risk of osteoporosis. Fractures are often the first symptom of osteoporosis after years of silent and progressive bone loss.

"We typically associate loss of bone mineral density with post-menopausal women, but our findings showed elevated risk in younger men," says Martha Ann Bass, PhD, Associate Professor of Health, Exercise Science and Recreational Management at University of Mississippi, and lead author on this study. "Almost all participants who were found to have osteopenia were surprised and I think this is a more prevalent issue than anyone expected."

In her study, Bass analyzed the bone mineral density of 173 adults between 35 and 50 years old. Participants were scanned at the femoral hip and lumbar spine, using dual-energy x-ray absorptiometry, which is proven to be precise, while exposing patients to a minimal dose of radiation.

Based on the findings, Bass believes more middle-aged adults should be scanned to understand their risk and establish a baseline for monitoring.

Keeping bones strong

Bone mineral density (BMD) is measured to determine bone health. Nutrition, lifestyle, environment, physical activity and genetics all contribute to BMD. Peak BMD is believed to be established by 30 years of age.

BMD decreases naturally with age, which means people who do not establish sufficiently strong bones as young adults are at increased risk for diseases like osteoporosis later in life.

Bass says the best way to maintain BMD is through weight-bearing exercises, like walking, running and jumping. Moderate weight lifting is also beneficial, though older adults are cautioned to maintain good form and avoid overly heavy weights.

Bass also noted that many of the men participating in her study had strong exercise habits, although a majority reported cycling as their workout of choice. Like swimming, cycling benefits the cardiovascular system but is not weight-bearing.

While a balanced diet is always important, patients may overestimate the value of calcium in maintaining bone health.

"Calcium plays a larger role when bones are still developing," says Bass. "After that, the body begins to rely on weight-bearing exercise to keep bones strong. It really does boil down to use it or lose it."

http://bit.ly/2EJdeMI

Could some chimpanzees' crustacean crave yield clues about human evolution?

First-ever evidence of wild chimps habitually catching and consuming freshwater crabs

Why do we fish? At some point eons ago, our primarily fruit-eating ancestors put their hands in the water to catch and eat aquatic life, inadvertently supplementing their diet with nutrients that initiated a brain development process that eventually led to humans. But how did this begin?

According to a research team from Kyoto University, one potential clue may have surfaced thanks to observations of humans' closest genetic relatives: chimpanzees. The scientists report the first-ever evidence of wild chimps habitually catching and consuming freshwater crabs. Writing in the *Journal of Human Evolution*, the team describes year-round, fresh water crab-fishing behavior—primarily among female and infant chimpanzees—living in the rainforest of the Nimba Mountains in Guinea, West Africa.

"The aquatic fauna our ancestors consumed likely provided essential long-chain polyunsaturated fatty acids, required for optimal brain growth and function," explains first author Kathelijne Koops from the University of Zurich and Kyoto University's Leading Graduate Program in Primatology and Wildlife Science.

"Further, our findings suggest that aquatic fauna may have been a regular part of hominins' diets and not just a seasonal fallback food."

The study began in 2012 when the researchers first observed the chimpanzees fishing for crabs. For two years, they documented the demographics and behavior of these chimps, while also analyzing and comparing the nutritional value of the crabs to other foods in the chimpanzees' diet.

Crabbing, they learned, not only took place year-round—without regard to season or fruit availability—but intriguingly was negatively correlated with the chimps' consumption of ants, another diet staple. Mature males were the least likely to consume aquatic fauna.

"Energy and sodium levels in large crabs are comparative with ants," explains Koops, "leading us to hypothesize that crabs may be an important year-round source of protein and salts for females—especially when pregnant or nursing—and for growing juveniles."

The study further sheds light on our own evolution, by showing that fishing behaviors may not be restricted by habitat as initially assumed.

"This isn't the first case of non-human primates eating crabs," points out senior co-author Tetsuro Matsuzawa, "but it is the first evidence of apes other than humans doing so. Notably, previous observations were from monkey species in locations consistent with

aquatic faunivory—lakes, rivers, or coastlines—and not in closed rainforest." "It's exciting to see a behavior like this that allows us to improve our understanding of what drove our ancestors to diversify their diet."

Kathelijne Koops et al. Crab-fishing by chimpanzees in the Nimba Mountains, Guinea, Journal of Human Evolution (2019). DOI: 10.1016/j.jhevol.2019.05.002

http://bit.ly/2wsHK99

Healthy fat hidden in dirt may fend off anxiety disorders

Lipid discovered in soil-dwelling bacteria helps explain 'hygiene hypothesis'

Thirty years after scientists coined the term "hygiene hypothesis" to suggest that increased exposure to microorganisms could benefit health, University of Colorado Boulder researchers have identified an anti-inflammatory fat in a soil-dwelling bacterium that may be responsible.

The discovery, published Monday in the journal Psychopharmacology, may at least partly explain how the bacterium, *Mycobacterium vaccae*, quells stress-related disorders. It also brings the researchers one step closer to developing a microbe-based "stress vaccine."

"We think there is a special sauce driving the protective effects in this bacterium, and this fat is one of the main ingredients in that special sauce," said senior author and Integrative Physiology Professor Christopher Lowry.

British scientist David Strachan first proposed the controversial "hygiene hypothesis" in 1989, suggesting that in our modern, sterile world, lack of exposure to microorganisms in childhood was leading to impaired immune systems and higher rates of allergies and asthma.

Researchers have since refined that theory, suggesting that it is not lack of exposure to disease-causing germs at play, but rather to "old friends" - beneficial microbes in soil and the environment - and that mental health is also impacted.

"The idea is that as humans have moved away from farms and an agricultural or hunter-gatherer existence into cities, we have lost contact with organisms that served to regulate our immune system and suppress inappropriate inflammation," said Lowry, who prefers the phrases 'old friends hypothesis' or 'farm effect.' "That has put us at higher risk for inflammatory disease and stress-related psychiatric disorders."

Lowry has published numerous studies demonstrating a link between exposure to healthy bacteria and mental health.

One showed that children raised in a rural environment, surrounded by animals and bacteria-laden dust, grow up to have more stress-resilient immune systems and may be at lower risk of mental illness than pet-free city dwellers.

Others have shown that when a particular bacterium, *Mycobacterium vaccae*, is injected into rodents, it alters the animals' behavior in a way similar to that of antidepressants and has long-lasting anti-inflammatory effects on the brain. Studies suggest exaggerated inflammation boosts risk of trauma- and stressor-related disorders, such as posttraumatic stress disorder (PTSD).

One recent Lowry-authored study, published in the Proceedings of the National Academy of Sciences in 2017, showed that injections of *M. vaccae* prior to a stressful event could prevent a "PTSD-like" syndrome in mice, fending off stress-induced colitis and making the animals act less anxious when stressed again later.

"We knew it worked, but we didn't know why," said Lowry. "This new paper helps clarify that."

For the new study, Lowry and his team identified, isolated and chemically synthesized a novel lipid, or fatty acid, called 10(Z)-hexadecenoic acid found in *Mycobacterium vaccae* and used next-

generation sequencing techniques to study how it interacted with macrophages, or immune cells, when the cells were stimulated.

They discovered that inside cells, the lipid acted like a key in a lock, binding to a specific receptor, peroxisome proliferator-activated receptor (PPAR), and inhibiting a host of key pathways which drive inflammation. They also found that when cells were pre-treated with the lipid they were more resistant to inflammation when stimulated.

"It seems that these bacteria we co-evolved with have a trick up their sleeve," said Lowry. "When they get taken up by immune cells, they release these lipids that bind to this receptor and shut off the inflammatory cascade."

Lowry has long envisioned developing a "stress vaccine" from *M. vaccae*, which could be given to first responders, soldiers and others in high-stress jobs to help them fend off the psychological damage of stress.

"This is a huge step forward for us because it identifies an active component of the bacteria and the receptor for this active component in the host," he said.

Simply knowing the mechanism of action by which *M. vaccae* reaps benefits could boost confidence in it as a potential therapeutic. And if further studies show the novel fat alone has therapeutic effects, that molecule could become a target for drug development, he said.

Overall, the study offers further proof that our "old friends" have a lot to offer.

"This is just one strain of one species of one type of bacterium that is found in the soil but there are millions of other strains in soils," Lowry said. "We are just beginning to see the tip of the iceberg in terms of identifying the mechanisms through which they have evolved to keep us healthy. It should inspire awe in all of us."

http://bit.ly/2QAMAu6

Experimental drug completely effective against Nipah virus

The experimental antiviral drug remdesivir completely protected four African green monkeys from a lethal dose of Nipah virus, according to a new study in Science Translational Medicine from National Institutes of Health scientists and colleagues.

First identified in 1999 in Malaysia, Nipah virus is an emerging pathogen found primarily in Bangladesh and India. The virus is spread to humans by fruit bats; person-to-person transmission also occurs. Nipah virus can cause neurological and respiratory disease; the mortality rate is about 70%. Delayed relapse, manifesting as brain inflammation or encephalitis, can occur. An outbreak in May 2018 in India resulted in 23 cases and 21 deaths.

Gilead Sciences, Inc., is developing remdesivir and, in collaboration with scientists from the Centers for Disease Control and Prevention (CDC), performed initial laboratory studies evaluating the drug against Nipah virus. Researchers from CDC and NIH's National Institute of Allergy and Infectious Diseases (NIAID) collaborated on the concept for the monkey study. NIAID then conducted the monkey studies with laboratory serology and pathology support from CDC. Animals infected with a lethal dose of Nipah virus received a first dose of intravenous remdesivir 24 hours after infection and then a daily intravenous dose for a total of 12 consecutive days. The NIAID team observed the animals for 92 days after infection, taking clinical samples 14 times during that span. The long period of observation allowed scientists adequate time to monitor the central nervous system for disease, which can be slow to develop when caused by Nipah virus. Two treated animals developed mild respiratory signs that resolved within three weeks; the other two treated animals showed no signs of illness. All four remained apparently healthy for the remainder of the study.

Four untreated animals also received a lethal dose of Nipah virus. They began showing signs of illness within four days of infection and rapidly developed fatal disease within eight days.

Scientists next plan to evaluate delayed drug administration to determine how long after infection the animals can be treated successfully. Remdesivir is the second experimental treatment, after monoclonal antibody m102.4, shown to prevent severe Nipah virus disease in a monkey model when administered after the animals are infected.

M. Lo et al. Remdesivir (GS-5734) protects African green monkeys from Nipah virus challenge. Science Translational Medicine DOI: 10.1126/scitranslmed.aau9242 (2019).

http://bit.ly/2MhPJAy

Seeing disfigured faces prompts negative brain and behavior responses

Penn brain imaging study finds negative implicit biases against individuals with scars, birthmarks and other facial differences

PHILADELPHIA--People with attractive faces are often seen as more trustworthy, socially competent, better adjusted, and more capable in school and work. The correlation of attractiveness and positive character traits leads to a "beautiful is good" stereotype. However, little has been understood about the behavioral and neural responses to those with facial abnormalities, such as scars, skin cancers, birthmarks, and other disfigurements. A new study led by Penn Medicine researchers, which published today in Scientific Reports, uncovered an automatic "disfigured is bad" bias that also exists in contrast to "beautiful is good."

"Judgements on attractiveness and trustworthiness are consistent across cultures, and these assumptions based on facial beauty are made extremely quickly. On the other hand, people with facial disfigurement are often targets of discrimination, which seems to extend beyond the specific effects of lower overall attractiveness and may tie in more with the pattern of results with stigmatized groups," said the study's lead author Anjan Chatterjee, MD, a professor of Neurology, and director of the Penn Center for Neuroaesthetics. "In order to right any discrimination, the first step is to understand how and why such biases exist, which is why we set out to uncover the neural responses to disfigured faces."

Neuroimaging studies show that seeing attractive faces evokes brain responses in reward, emotion, and visual areas compared to seeing faces of average attractiveness. Specifically, attractive faces evoke greater neural responses as compared to faces of average attractiveness in ventral occipito-temporal cortical areas, which process faces and other objects. Additionally, attractiveness correlates with increased activations in the anterior cingulate cortex and medial-prefrontal cortex--areas which are associated with rewards, empathy, and social cognition.

The researchers set out to evaluate the behavioral and brain reactions to disfigured faces and investigate whether surgical treatment mitigates these responses. In two experiments, the researchers used a set of photographs of patients with different types of facial anomalies, before and after surgical treatment, to test whether people harbor a "disfigured is bad" bias and to measure neural responses.

In the first experiment, a behavioral study with 79 participants, the researchers tested if people harbor implicit biases against disfigured faces and if such implicit biases were different from consciously aware, self-reported explicit biases. The behavioral experiment consisted of an implicit association test (IAT) and an explicit bias questionnaire (EBQ) to identify whether people have a negative bias for disfigured faces. For the IAT, the researchers used the set of before and after photographs as a stimulus. The EBQ consisted of 11 questions which query conscious biases against people with facial disfigurements. While the team found no indication of an

explicit bias, they found that non-disfigured faces were preferred in the IAT. This bias was particularly robust for men.

In a follow up functional MRI (fMRI) study with 31 participants, researchers tested brain responses to the same picture pairs. Participants judged the gender of each photograph they viewed. The researchers found increased neural responses in visual regions of the brain (the ventral occipito-temporal cortical areas) and decreases in regions associated with empathy (the anterior cingulate and medio-prefrontal cortex).

In sum, the authors found that people have implicit negative biases against people with disfigured faces, without knowingly harboring such biases. The diminished neural responses in the anterior cingulate cortex suggests that people are less empathetic when looking at individuals with disfigurement--this is also a potential neural marker of dehumanization, as diminished neural responses in the anterior cingulate cortex is also observed in response to other stigmatized people, such as the homeless and drug addicts.

"The emphasis of attractiveness and its association with positive attributes highlights the pervasive effect of appearance in social interaction. Chatterjee said. "While we found that corrective surgery mitigates negative social and psychological responses to people with facial anomalies, we are also exploring alternative strategies to minimize bias towards people with facial conditions."

This work was supported by the Penn Center for Human Appearance and the Global Wellness Institute.

http://bit.ly/2WCkvbp

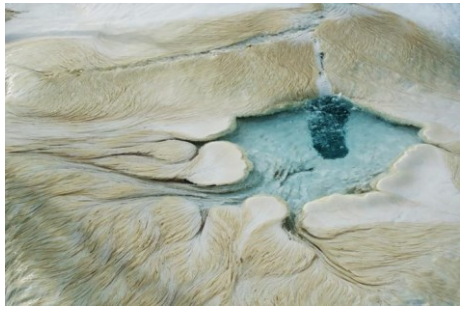
'Fettuccine' may be most obvious sign of life on Mars, researchers report

***A rover scanning the surface of Mars for evidence of life might want to check for rocks that look like pasta, researchers report in the journal* Astrobiology.**

CHAMPAIGN, Ill. -- The bacterium that controls the formation of such rocks on Earth is ancient and thrives in harsh environments that are similar to conditions on Mars, said University of Illinois geology professor Bruce Fouke, who led the new, NASA-funded study.

"It has an unusual name, *Sulfurihydrogenibium yellowstonense*," he said. "We just call it 'Sulfuri.'"

The bacterium belongs to a lineage that evolved prior to the oxygenation of Earth roughly 2.35 billion years ago, Fouke said. It can survive in extremely hot, fast-flowing water bubbling up from underground hot springs. It can withstand exposure to ultraviolet light and survives only in environments with extremely low oxygen levels, using sulfur and carbon dioxide as energy sources.



New research reveals that the bacterium *Sulfurihydrogenibium yellowstonense* thrives in harsh environments with conditions like those expected on Mars. Photo by Tom Murphy

"Taken together, these traits make it a prime candidate for colonizing Mars and other planets," Fouke said.

And because it catalyzes the formation of crystalline rock formations that look like layers of pasta, it would be a relatively easy life form to detect on other planets, he said.

The unique shape and structure of rocks associated with Sulfuri result from its unusual lifestyle, Fouke said. In fast-flowing water, Sulfuri bacteria latch on to one another "and hang on for dear life," he said.

"They form tightly wound cables that wave like a flag that is fixed on one end," he said. The waving cables keep other microbes from attaching. Sulfuri also defends itself by oozing a slippery mucus.

"These Sulfuri cables look amazingly like fettuccine pasta, while further downstream they look more like capellini pasta," Fouke said. The researchers used sterilized pasta forks to collect their samples from Mammoth Hot Springs in Yellowstone National Park.

The team analyzed the microbial genomes, evaluated which genes were being actively translated into proteins and deciphered the organism's metabolic needs, Fouke said.

The team also looked at Sulfuri's rock-building capabilities, finding that proteins on the bacterial surface speed up the rate at which calcium carbonate - also called travertine - crystallizes in and around the cables "1 billion times faster than in any other natural environment on Earth," Fouke said. The result is the deposition of broad swaths of hardened rock with an undulating, filamentous texture. "This should be an easy form of fossilized life for a rover to detect on other planets," Fouke said.

"If we see the deposition of this kind of extensive filamentous rock on other planets, we would know it's a fingerprint of life," Fouke said. "It's big and it's unique. No other rocks look like this. It would be definitive evidence of the presences of alien microbes."

Fouke also is an affiliate professor of microbiology and of the Carl R. Woese Institute for Genomic Biology at the U. of I.

The paper "Physiology, metabolism, and fossilization of hot-spring filamentous microbial mats" is available online and from the U. of I. News Bureau.

http://bit.ly/2XhqVR3

Early onset colorectal cancer rising fastest in the west

Surprising finding suggests obesity epidemic may not fully explain increasing rates

Early-onset colorectal cancer -cancer occurring before age 50--is rising most rapidly in Western states, where healthy behaviors are prominent, according to a new study. The authors of the study, which appears in the *Journal of the National Cancer Institute*, say the findings indicate the need for further etiologic studies to explore early-life colorectal carcinogenesis.

Early-onset colorectal cancer (CRC) has been on the rise for several decades in the United States for unknown reasons. Because geographic differences could help uncover potential causes for the trend, investigators at the American Cancer Society and The Ohio State University analyzed changes in CRC incidence and risk factors among adults under 50 during 1995-2015 by state and race/ethnicity.

Based on cancer registries representing 95% of the US population, the study found early-onset CRC incidence increased over the most recent ten data years (2006-2015) by 1.1% per year. Rates rose faster for rectal tumors (1.7% per year) than for colon tumors (0.7% per year).

The increase was mostly confined to whites, among whom rates rose in 40 out of 47 states (with available data) and were otherwise stable. The rise varied in magnitude across states, with average increases exceeding 2.5% per year in ten states, six of which are in the West. For example, over the past two decades CRC incidence increased by 73% in Washington, from 6.7 (per 100,000) during 1995-1996 to 11.5 during 2014-2015, and by 57% in Colorado, from 6.0 to 9.5. Increases were generally steeper for rectal than for colon cancer, with rates doubling in some states (e.g. in Colorado, from 1.9 to 4.2), converging with rates for colon cancer.

"Although early-onset colorectal cancer incidence is currently lowest in Western states and highest in Southern states, consistent with the prevalence of established risk factors, like obesity, physical inactivity, and smoking, this pattern may change because the steepest increases are in Western states," said Rebecca L. Siegel, MPH, American Cancer Society scientific director of surveillance research and lead author of the study. "This finding suggests that early life exposures in addition to the 'usual suspects ' may be contributing to the rise in early onset disease. Future studies should explore novel risk factors for colorectal cancer in young adults."

Article: State variation in early-onset colorectal cancer in the United States, 1995-2015, RL Siegel, GA Medhanie, SA Fedewa, A Jemal; J Nat Can Inst *2019 doi: 10.1093/jnci/djz098*
URL upon publication: https://doi.org/10.1093/jnci/djz098

http://bit.ly/2HO8t6H

Neanderthals May Have Been Driven to Extinction by a Tiny Drop in Fertility Rates

Neanderthals could have gone extinct due to a slight drop in their fertility rates, a new study finds.

By Charles Q. Choi, Live Science Contributor

The last of the Neanderthals, the closest extinct relatives of modern humans, disappeared from Europe about 40,000 years ago. Previous research estimated that at its peak, the entire Neanderthal population in both Europe and Asia was quite small, totaling 70,000 at most.

A sculpture of a Neanderthal woman located at the National Archaeological Museum of Madrid. New research suggests just a 2% drop in fertility rates could have driven Neanderthals to extinction. **Credit: Shutterstock**

Scientists have long debated whether the dispersal of modern humans across the globe helped kill off Neanderthals, either directly through conflict or indirectly through the spread of disease.

"The disappearance of the Neanderthal population is an exciting subject — imagine a human group that has lived for thousands of years and is very well-adapted to its environment, and then disappears," study senior author Silvana Condemi, a paleoanthropologist at Aix-Marseille University in Marseille, France, told Live Science. "For a long time, it was thought that *Homo sapiens* had simply killed the Neanderthals. Today, thanks to the results of genetic analysis, we know that the encounters between Neanderthals and sapiens were not always so cruel, and that interbreeding took place — even today's humans have genes of Neanderthal origin."

Instead of investigating why the Neanderthals disappeared, "we looked for the 'how' of their demise," Condemi said. Specifically, the scientists generated computer models that explored how Neanderthal populations might decline and go extinct over time in response to a variety of factors, such as war, epidemics and reduced fertility or survival rates among men and women of varying ages.

"Very quickly, we found something unexpected — this disappearance, which occurred over a very long period, cannot be explained by a catastrophic event," Condemi said. Computer models that assumed modern humans killed off Neanderthals via war or epidemics found that these factors would have driven Neanderthals to extinction far more rapidly than the 4,000 to 10,000 years in the archaeological record during which modern humans and Neanderthals are known to have coexisted in Europe, the researchers said.

The scientists also found that neither an increase in juvenile or adult survival rates, nor a strong decrease in fertility rates, were likely causes for the long decline seen in Neanderthals. Instead, they discovered that Neanderthal extinction was possible within 10,000 years with a 2.7% decrease in fertility rates of young Neanderthal women — first-time mothers less than 20 years old — and within 4,000 years with an 8% decrease in fertility rates in this same group.

"The disappearance of the Neanderthals was probably due to a slight decline in the fertility among the youngest women," Condemi said. "This is a phenomenon that is limited in scope that, over time, had an impact."

A variety of factors might have lowered these fertility rates. Condemi noted that pregnancies among young, first-time mothers "are on the average more risky than second or later pregnancies. A minimum of calories is essential for the maintenance of pregnancy,

and a reduction of food, and therefore of calories, is detrimental to pregnancy." Neanderthals disappeared during a time of climate change. Environmental fluctuations might have led to a slight decrease in food, and in turn "may explain a reduction in fertility," Condemi said.

Condemi noted that prior work suggested that with modern humans "if the average number of births falls to a level of 1.3 among the women of the world, our species would disappear in 300 years. This is an unlikely model, but the results would be very rapid!"

The scientists detailed their findings online May 29 in the journal PLOS ONE.

http://bit.ly/2W9yIsq

Early statin treatment may help children with Fragile X

Children with an inherited form of intellectual disability and autism could be helped by a medicine commonly used to lower cholesterol, if used early in life.

The drug - called lovastatin - corrected learning and memory problems in rats with a form of Fragile X Syndrome, tests revealed.

Rats were treated with lovastatin for four weeks during infancy but the benefits persisted for months afterwards.

Researchers say this suggests learning problems in children with Fragile X might be prevented by a similar treatment in early life.

Fragile X Syndrome is one of the most common genetic causes of intellectual disability. It is often associated with autism and attention deficit and hyperactivity disorder, or ADHD. Many affected individuals also have seizures.

The condition occurs when a particular gene is disrupted leading to altered communication between brain cells.

Previous studies in mice and rats have shown that this disruption can be treated with drugs, but it was not known how long treatment might be effective for.

Researchers at the University of Edinburgh studied rats with a genetic alteration similar to that found in people with Fragile X Syndrome. These rats have problems completing certain memory tasks when compared with typical rats.

Treatment with lovastatin between five and nine weeks of age - the precise window when they are developing these memory abilities - restored normal development in the rats.

The animals were able to complete the memory tasks more than three months after treatment ended, indicating the effects of the drug were long-lasting.

Children with Fragile X Syndrome are usually diagnosed around the age of three, typically because they are late in learning to speak. Genetic tests have enabled earlier diagnosis, which raises the possibility of starting treatments sooner.

Current medications help manage specific symptoms - such as hyperactivity and seizures - but there are not yet any treatments that tackle the underlying brain changes leading to Fragile X Syndrome.

Statins are widely prescribed to both children and adults to control high blood cholesterol and to reduce the risk of heart disease.

The study, published in *Science Translational Medicine*, was led by researchers at the University of Edinburgh's Patrick Wild Centre and the Simons Initiative for the Developing Brain.

Professor Peter Kind, Director of the Patrick Wild Centre and Simons Initiative for the Developing Brain at the University of Edinburgh, said: "Children with Fragile X Syndrome need special education and, although some will live semi-independently, most require some form of lifelong support.

"We have found that early intervention for a limited period during development can lead to persistent beneficial effects, long after treatment ends, in a rat model of Fragile X Syndrome. Our future experiments will focus on whether there is a critical time-window during development when treatment is more effective."

http://bit.ly/2JObbv6

Scientists find telling early moment that indicates a coming megaquake

Just 10 seconds into a quake, GPS data can detect signs of acceleration that point to an event's magnitude, says a University of Oregon researcher

EUGENE, Ore. - Scientists combing through databases of earthquakes since the early 1990s have discovered a possible defining moment 10-15 seconds into an event that could signal a magnitude 7 or larger megaquake.

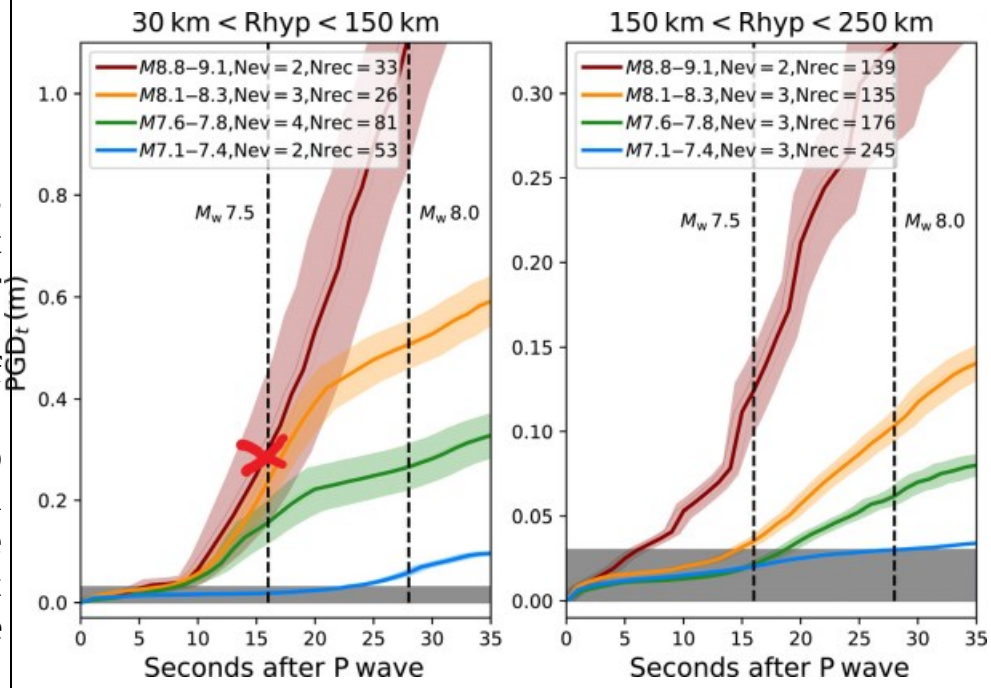
Likewise, that moment - gleaned from GPS data on the peak rate of acceleration of ground displacement - can indicate a smaller event.

GPS picks up an initial signal of movement along a fault similar to a seismometer detecting the smallest first moments of an earthquake. Such GPS-based information potentially could enhance the value of earthquake early warning systems, such as the West Coast's ShakeAlert, said Diego Melgar, a professor in the Department of Earth Sciences at the University of Oregon.

The physics-heavy analyses of two databases maintained by co-author Gavin P. Hayes of the U.S. Geological Survey's National Earthquake Information Center in Colorado detected a point in time where a newly initiated earthquake transitions into a slip pulse where mechanical properties point to magnitude.

Melgar and Hayes also were able to identify similar trends in European and Chinese databases. Their study was detailed in the May 29 issue of the online journal Science Advances.

"To me, the surprise was that the pattern was so consistent, Melgar said. "These databases are made different ways, so it was really nice to see similar patterns across them." Overall, the databases contain data from more than 3,000 earthquakes. Consistent indicators of displacement acceleration that surface between 10-20 seconds into events were seen for 12 major earthquakes occurring in 2003-2016.



Scientists have found in GPS data a telling window that begins 10 seconds into an earthquake. In four sample events (colored lines), the acceleration of peak ground displacement (measurements shown at right) just five seconds later suggests whether a megaquake, such as a magnitude 9 (red X) or a sub-7 magnitude quake is in progress. Real time monitoring, the researchers say, could enhance earthquake early warning. **University of Oregon**

GPS monitors exist along many land-based faults, including at ground locations near the 620-mile-long Cascadia subduction zone off the U.S. Pacific Northwest coast, but their use is not yet common in real time hazard monitoring. GPS data shows initial movement in centimeters, Melgar said.

"We can do a lot with GPS stations on land along the coasts of Oregon and Washington, but it comes with a delay," Melgar said. "As an earthquake starts to move, it would take some time for

information about the motion of the fault to reach coastal stations. That delay would impact when a warning could be issued. People on the coast would get no warning because they are in a blind zone." This delay, he added, would only be ameliorated by sensors on the seafloor to record this early acceleration behavior.

Having these capabilities on the seafloor and monitoring data in real time, he said, could strengthen the accuracy of early warning systems. In 2016, Melgar, as a research scientist at Berkeley Seismological Laboratory in Berkeley, California, led a study published in Geophysical Research Letters that found real time GPS data could provide an additional 20 minutes of warning of a possible tsunami.

Japan already is laying fiber optic cable off its shores to boost its early warning capabilities, but such work is expensive and would be more so for installing the technology on the seafloor above the Cascadia fault zone, Meglar noted.

Melgar and Hayes came across the slip-pulse timing while scouring USGS databases for components that they could code into simulations to forecast what a magnitude 9 rupture of the Cascadia subduction zone would look like. The subduction zone, which hasn't had a massive lengthwise earthquake since 1700, is where the Juan de Fuca ocean plate dips under the North American continental plate. The fault stretches just offshore of northern Vancouver Island to Cape Mendocino in northern California.

http://bit.ly/2QDcAVL

Could Squeezing Your Arms and Legs Help Prevent Strokes?

A simple squeeze to your arms and legs might benefit your brain — turns out, the added pressure may improve the regulation of blood flow to your brain as well as levels of stroke-protective molecules, a new study suggests.

By Yasemin Saplakoglu, Staff Writer

The study found that people who wore an inflated blood pressure cuff on one arm and leg for minutes at a time experienced more controlled blood flow to their brains. This method also increased molecules in the blood previously suggested to play a protective role in the brain, such as in preventing stroke, a group of researchers reported today (May 29) in the journal Neurology.

Previous research has suggested that "training" organs by restricting blood flow — and therefore oxygen — to them through periodically compressing the arms and legs may make them more resilient when problems arise.

For example, a trained heart may be more resistant to changes in blood flow during a heart attack. And such training may allow the brain to better regulate that organ's blood flow despite changes in blood pressure, a process called "cerebral autoregulation," the authors said.

"It is generally believed that impairment of cerebral autoregulation may increase the risk of brain injury, especially stroke," said study senior author Dr. Yi Yang, a neurologist at the First Hospital of Jilin University in China. "And there is currently no report on how to improve cerebral autoregulation in order to reduce the risk."

The researchers are optimistic that these simple compressions to the arms and legs may help reduce the risk of stroke, but much more research will be needed before any conclusions about stroke prevention can be drawn.

Training the body

In the new study, the researchers enrolled nearly 50 healthy people who were, on average, 35 years of age. Each person went through two consecutive days of blood pressure monitoring. On the second day, they were hooked up to blood pressure cuffs, one on the upper arm and one on the thigh.

The blood pressure cuff was inflated for 5 minutes and then deflated for 5 minutes, and this process was repeated four times.

The researchers took participants' blood pressure at the start of the day and periodically throughout the next 24 hours.

They found that 6 hours after having the cuff compressions, people had improved cerebral autoregulation, which remained improved for at least 18 hours. The researchers measured cerebral autoregulation in part by using an ultrasound to measure blood flow within the brain's two main arteries.

The scientists also took blood samples at the start of each day and 1 hour after the compressions. They found that an hour after the compressions, the participants had increased numbers of certain biomarkers — molecules that act like signals pointing to the presence of a condition in the body — compared with their levels before the experiment.

Specifically, they found an increase in two biomarkers known to protect the nervous system. One of them, called the "glial cell line-derived neurotrophic factor," has been previously found to promote cell survival and help regenerate and restore damaged neurons.

They also found significant changes in the levels of biomarkers involved in regulating inflammation in the body. Inflammation is thought to play a role in a host of diseases, from diabetes and heart disease to Alzheimer's and depression. However, some of these markers promote inflammation, and some are anti-inflammatory, and it's unclear how changes to these markers might be beneficial or not to the brain, the authors reported.

Stroke prevention

"Although we cannot draw conclusions that [this intervention] can prevent stroke ... we still are optimistic," Yang told Live Science. The researchers note that the preventative effects aren't proven and though this appears to be relatively safe, they don't recommend people try this on their own without talking to their doctors.

This study "gives us a unique insight into how some of our patients with multiple stroke risk factors seem to avoid devastation with the inevitable onset of ischemic stroke," Dr. Paul Nyquist, a neurologist at Johns Hopkins University School of Medicine, and Dr. Marios Georgakis, a researcher at the Ludwig Maximilians University of Munich, wrote in an editorial accompanying the study. Neither of the editorial authors was involved with the study.

However, they note that this study was conducted on relatively young and healthy people and the results shouldn't be extrapolated to older adults or those with vascular diseases. "Thus, individuals with cerebrovascular disease who might actually benefit may not have the observed" response to the blood pressure cuff, they wrote.

Yang and the team hope to conduct follow-up studies to understand if these compressions might also help patients or subjects with a high risk of stroke.

http://bit.ly/2wvTDuT

New Virus Infecting People in China, and Ticks May Be the Culprit

Newly discovered virus found infecting people in China may be transmitted by ticks

By Rachael Rettner, Senior Writer

A newly discovered virus has been found infecting people in China, and it may be transmitted by ticks, according to a new report.

Researchers have dubbed the virus "Alongshan virus" after the town in northeastern China where it was first discovered, according to the report, published yesterday (May 29) in the New England Journal of Medicine. In humans, the virus is linked to a number of symptoms, including fever, headache and fatigue, and in some cases, nausea, rash and even coma.

The taiga tick, shown above, was found to harbor a newly-discovered virus in China. **Shutterstock**

So far, the virus has been found only in northeastern China, but it could potentially have a much wider range, experts say.

The 'first' patient

The virus was first identified in a 42-year-old farmer from Alongshan who became mysteriously ill with a fever, headache and nausea; he visited a hospital in the region of Inner Mongolia in April 2017. The farmer also reported a history of tick bites. At first, doctors thought the patient was infected with tickborne encephalitis virus (TBEV), another virus that's spread by ticks and is endemic to the region.

But the patient tested negative for TBEV, leading the researchers to look for other causes. Further research revealed that the patient was infected with a virus that is genetically distinct from other known viruses, the report said.

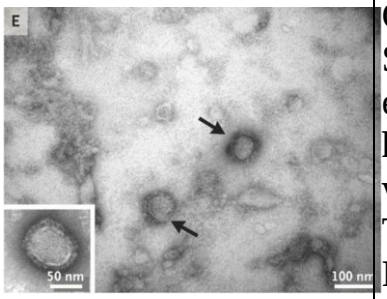


Image showing the Alongshan virus particles (arrows). **The New England Journal of Medicine ©2019**

After identifying the virus, the researchers began examining blood samples from other patients who visited their hospital with similar symptoms, and reported a history of tick bites. They found that, of the 374 patients who visited the hospital over the following five months and met this criteria, 86 patients were infected with the Alongshan virus. Nearly all of these patients were farmers or forestry workers, the report said.

When the researchers tested ticks and mosquitoes in the region, they found the virus was present in both insects.

Where is the virus found?

The researchers suspect the virus is transmitted by the taiga tick (*Ixodes persulcatus*), which is found in parts of eastern Europe and Asia, including China, Korea, Japan, Mongolia and Russia. Still, the study can't prove this tick does indeed transmit the disease, and can't rule out the possibility that mosquitoes are transmitting the disease, the authors said.

Laura Goodman, an assistant research professor at Cornell University's College of Veterinary Medicine in Ithaca, New York, called the new work an "excellent study," but said it leaves some unanswered questions. Critically, researchers will need to confirm which disease "vectors" are able to transmit the disease to people. "Until we can really know the answer to that question, we can't fully confirm the potential geographic range" of the virus, Goodman told Live Science.

Still, the researchers of the new study were able to characterize the entire genome of the Alongshan virus, and this information will help in broader surveillance for the virus, said Goodman, who wasn't involved with the study.

The Alongshan virus belongs to a family of viruses called Flaviviridae, the same family that includes TBEV as well as mosquito-borne viruses, such as dengue fever, West Nile virus, and Zika virus, according to the Centers for Disease Control and Prevention (CDC). The Alongshan virus is most closely related to another tickborne virus, called the Jingmen tick virus, which was first discovered in 2014.

If the taiga tick does turn out to transmit the Alongshan virus, then the range of the virus could potentially include the entire range of that tick, Goodman said. In addition, the virus might be found in other parts of the world — including other continents — if it can be transmitted by other types of ticks. Goodman noted that the closely related Jingmen tick virus has been found in both China and parts of Central and South America.

Goodman also noted that the Asian longhorned tick (*Haemaphysalis longicornis*), which is native to Asia and has recently shown up in the United States, can also carry the Jingmen tick virus. However, there's no evidence that the Asian longhorned

tick can carry the Alongshan virus. And in the U.S., the Asian longhorned tick has not been found to transmit any diseases.

In the new study, all 86 patients were treated based on their symptoms with a combination of an antiviral and antibiotic drug; their symptoms went away in about 6 to 8 days of treatment. Patients spent an average of 10 to 14 days in the hospital; and all of the patients eventually recovered without any long-term complications, the report said.

"Our findings suggest that [the Alongshan virus] may be the cause of a previously unknown febrile disease, and more studies should be conducted to determine the geographic distribution of this disease outside its current areas of identification," the authors concluded.

http://bit.ly/2EO3v7T

Researchers restore beta-cell function by deleting old cells

Acceleration of beta-cell aging determines diabetes -- senolysis improves

BOSTON - Research from Joslin Diabetes Center has shown in mice that insulin resistance increases the proportion of aged beta-cells which are dysfunction. Such an increase in aged beta-cells could lead to type 2 diabetes. These researchers confirmed similarly increased proportion of aged beta-cells in islets recovered from humans with type 2 diabetes. The study also showed that beta cell function can be recovered by removing these aged populations either via genetic modification or oral medication.

"Our hypothesis was that there was an important component in the development of diabetes which consisted of accelerated aging of beta-cells and that this population could be targeted therapeutically," says Cristina Aguayo-Mazzucato, MD, PhD, Assistant Investigator in the Section on Islet Cell and Regenerative Biology, first author on the paper, recently published in Cell Metabolism.

This research falls into a broader field of the study of senescence. Senescence is the slow decline of proliferation and function of a specific cell population. These cells accumulate as organisms grow older, but certain circumstances can cause some cells in an organism to age faster than the whole.

The research team, led by Dr. Aguayo-Mazzucato, generated animal models of insulin resistance and tracked the proportion of senescent beta-cells.

"What we found is that indeed, insulin resistance was increasing the amount of senescent or old beta-cells," she says.

Next, they deleted the aged cells through either genetic manipulation or medications that are known to remove senescent cells. The results were striking.

"We were able to recover beta cell function, we were able to restore glucose tolerance," says Dr. Aguayo-Mazzucato

The ability to restore beta cell function with minimal intervention could be a game changer in the care of type 2 diabetes. For many people with the disease, beta cell function declines to the point where they need injectable insulin. Should this research be borne out in clinic trials, the implications for treatment could be huge.

"When you look at the absolute percentage or quantity of the senescent beta-cells, they rarely exceed 20 percent of the whole beta cell population and yet targeting this relatively minor population had a huge effect on function and glucose metabolism and cellular identity," she says.

Medications to delete senescent cells , termed senolytics, are still under investigation. Dr. Aguayo-Mazzucato and her team hope to bring a potential treatment closer to the clinic by partnering with companies that are already working on senolytics, to test if their medications would work for people with diabetes.

"This opens a new target to treat diabetes which is basically to target populations of old or senescent cells that are really contributing to the local disfunction," she says.

Senolysis, or the removal of aged or dysfunctional cells, is a growing field in the treatment of age-related diseases. This new research fits into the larger picture of how senolytics could help combat many different diseases of aging, leading to better quality of life.

"In fact, it's a very exciting and rapidly growing field in medicine, which is called Senolytics or Senolysis," says Dr. Aguayo-Mazzucato. "It has promises, as shown by other laboratories, in osteoarthritis, muscle frailty or degeneration, renal function, some brain function."

While the work was completed in models of type 2 diabetes, the findings could also be relevant in type 1 diabetes.

"What we're seeing is that senescence is, in reality, a response to stress. In the case of type two diabetes, this stress is insulin resistance. In the case of type one diabetes, it is the immune attack on beta-cells," she says. "But in both models, beta-cells are responding to these stresses by becoming senescent. So, we think that the potential of this new vision of preventing diabetes will be valid for both type one and type two."

Joshua Andle, Terrence B Lee Jr, Ayush Midha, Lindsay Talemal, Vaja Chipashvili, Jennifer Hollister-Lock, Jan van Deursen, Gordon Weir and Susan Bonner-Weir also contributed to the paper.

This study was supported by grants from the National Institutes of Health (NIH), the Diabetes Research and Wellness Foundation, and an important group of private donors.

http://bit.ly/2wHpTvv

Acid, wasabi, chillies: mole-rats couldn't give a toss

Several species of African rodent display remarkable insensitivity to pain, hinting at new ways to manage it in humans.

Paul Biegler reports.

Scientists have discovered that a half-blind African mole-rat can take about as much wasabi as you can throw at it, for reasons that could lead to new painkillers in humans.

The team, led by Gary Lewin at the Max Delbrück Centre for Molecular Medicine in Berlin, Germany, and including colleagues in South Africa and Tanzania, co-opted nine species of mole-rat, from three families in a test of culinary-oriented pain sensitivity.

The burrowing, buck-toothed natives of East Africa were given paw injections of capsaicin, the compound responsible for the burning sensation of chillies, and allyl isothiocyanate (AITC), which delivers the eye-watering hit of wasabi, the Japanese condiment often eaten with sushi.

For good measure the animals also got a dose of hydrochloric acid.

Meet the highveld mole-rat (Cryptomys hottentotus pretoriae), a species that would win a wasabi-eating contest paws down. **Jane Reznick**

To see if the critters felt any pain, the team measured how long they spent lifting and licking the affected limb.

Two species were insensitive to the acid, one to capsaicin, and a fourth, the unfortunate-looking naked mole rat (*Heterocephalus glaber*), displayed a distinct lack of pain to both. Only one rat, however, could hack AITC which, it is worth noting, also gives mustard and horseradish their distinctive punch.

The animal in question was the highveld mole-rat (*Cryptomys hottentotus pretoriae*) which, the researchers report, was "completely insensitive to AITC". A big question is why.

As it happens, AITC is found in plant roots that form a major part of the highveld mole-rat's diet, so the ability to eat them without a fuss may have emerged as an evolutionary advantage. But an even

bigger question, and one that should have pain researchers pricking up their ears, is how the species pulls off its wasabi-beating trick.

To find out, the team looked at genes expressed in part of the rat's pain-sensing system, the dorsal root ganglia, where sensory nerves connect with the spinal cord to take pain messages to the brain.

They found that one gene, called *Nalcn*, was present at levels six times higher in the highveld mole-rat than in other species sensitive to AITC. *Nalcn*, as it happens, controls the entry of sodium into nerve cells; when there is a lot of it, the nerve cells become leaky to sodium, fire less and get worse at taking pain messages to the brain.

The pain-busting properties of overactive *Nalcn* looked to confer wasabi resistance. But the researchers also wondered if they might explain another curious behaviour of the animal. It shares its burrow with a species that all other mole-rats avoid like the plague; the Natal droptail ant (*Myrmicaria natalensis*).

"These insects are known for their aggressive nature and highly pungent venom," says Lewin. If the highveld mole-rat were impervious to the ant's bite, it might get a survival edge by being able to cohabit with them. But how to test the theory?

Continuing the gastronomic vein, the researchers came up with a nasty concoction made from the crushed abdomens of the ants. Applied to the paws of two mole-rat species, that sting syrup led to some serious lifting and licking. But the same syrup on the paw of the highveld mole-rat was met with indifference.

Up-regulated *Nalcn* in the species also seemed to confer insensitivity to the ant bite. The researchers, however, needed one final check to be sure.

Verapamil is a drug used for heart conditions and it also blocks the *Nalcn*-controlled sodium channels in rats. Dosed with it, the highveld mole-rats were now dancing in pain from the ant syrup, something of a slam dunk for the theory that *Nalcn*, and sodium channels in nerves, are really important in transmission of pain signals. "From the thousands of genes we were looking at, we had obviously found the very gene responsible for the highveld mole-rat's remarkable pain resistance," says Lewin. Which could be very good news for a certain larger species.

"This discovery could well lead to the development of highly effective analgesics," says Lewin.

The research is published in the journal *Science*.

http://bit.ly/2QGBm7n

Transgenic fungus rapidly killed malaria mosquitoes in West African study

Technology developed at the University of Maryland could safely reduce malaria mosquito populations, including insecticide-resistant strains

According to the World Health Organization, malaria affects hundreds of millions of people around the world, killing more than 400,000 annually. Decades of insecticide use has failed to control mosquitoes that carry the malaria parasite and has led to insecticide-resistance among many mosquito strains. In response, scientists began genetically modifying mosquitoes and other organisms that can help eradicate mosquitoes. Until now, none of these transgenic approaches made it beyond laboratory testing.

In a research paper published in the May 31, 2019, issue of the journal Science, a team of scientists from the University of Maryland and Burkina Faso described the first trial outside the laboratory of a transgenic approach to combating malaria. The study showed that a naturally occurring fungus engineered to deliver a toxin to mosquitoes safely reduced mosquito populations by more than 99% in a screen-enclosed, simulated village setting in Burkina Faso, West Africa.

"No transgenic malaria control has come this far down the road toward actual field testing," said Brian Lovett, a graduate student in UMD's Department of Entomology and the lead author of the paper.

"This paper marks a big step and sets a precedent for this and other transgenic methods to move forward."

"We demonstrated that the efficacy of the transgenic fungi is so much better than the wild type that it justifies continued development," said Raymond St. Leger, a Distinguished University Professor of Entomology at UMD and co-author of the study.

The fungus is a naturally occurring pathogen that infects insects in the wild and kills them slowly. It has been used to control various pests for centuries. The scientists used a strain of the fungus that is specific to mosquitoes and engineered it to produce a toxin that kills mosquitoes more rapidly than they can breed. This transgenic fungus caused mosquito populations in their test site to collapse to unsustainable levels within two generations. "You can think of the fungus as a hypodermic needle we use to deliver a potent insect-specific toxin into the mosquito," said St. Leger.

The toxin is an insecticide called Hybrid. It is derived from the venom of the Australian Blue Mountains funnel-web spider and has been approved by the Environmental Protection Agency (EPA) for application directly on crops to control agricultural insect pests.

"Simply applying the transgenic fungus to a sheet that we hung on a wall in our study area caused the mosquito populations to crash within 45 days," Lovett said. "And it is as effective at killing insecticide-resistant mosquitoes as non-resistant ones."

Lovett said laboratory tests suggest that the fungus will infect the gamut of malaria-carrying mosquitoes. The abundance of species that transmit malaria has hindered efforts to control the disease, because not all species respond to the same treatment methods.

To modify the fungus Metarhizium pingshaense so that it would produce and deliver Hybrid, the University of Maryland research team used a standard method that employs a bacterium to intentionally transfer DNA into fungi. The DNA the scientists designed and introduced into the fungi provided the blueprints for making Hybrid along with a control switch that tells the fungus when to make the toxin.

The control switch is a copy of the fungus' own DNA code. Its normal function is to tell the fungus when to build a defensive shell around itself so that it can hide from an insect's immune system. Building that shell is costly for the fungus, so it only makes the effort when it detects the proper surroundings--inside the bloodstream of a mosquito.

By combining the genetic code for that switch with the code for making Hybrid, the scientists were able to ensure that their modified fungus only produces the toxin inside the body of a mosquito. They tested their modified fungus on other insects in Maryland and Burkina Faso, and found that the fungus was not harmful to beneficial species such as honeybees.

"These fungi are very selective," St. Leger said. "They know where they are from chemical signals and the shapes of features on an insect's body. The strain we are working with likes mosquitoes. When this fungus detects that it is on a mosquito, it penetrates the mosquito's cuticle and enters the insect. It won't go to that trouble for other insects, so it's quite safe for beneficial species such as honeybees."

After demonstrating the safety of their genetically modified fungus in the lab, Lovett and St. Leger worked closely with scientific colleagues and government authorities in Burkina Faso to test it in a controlled environment that simulated nature. In a rural, malaria-endemic area of Burkina Faso, they constructed a roughly 6,550-square-foot, screened-in structure they called MosquitoSphere. Inside, multiple screened chambers contained experimental huts, plants, small mosquito-breeding pools and a food source for the mosquitoes.

In one set of experiments, the researchers hung a black cotton sheet coated with sesame oil on the wall of a hut in each of three

chambers. One sheet received oil mixed with the transgenic fungus Metarhizium pingshaense, one received oil with wild-type Metarhizium and one received only sesame oil. Then, they released 1,000 adult male and 500 adult female mosquitoes into each chamber of MosquitoSphere to establish breeding populations. The researchers then counted mosquitoes in each chamber every day for 45 days.

In the chamber containing the sheet treated with the transgenic fungus, mosquito populations plummeted over 45 days to just 13 adult mosquitoes. That is not enough for the males to create a swarm, which is required for mosquitoes to breed. By comparison, the researchers counted 455 mosquitoes in the chamber treated with wild-type fungus and 1,396 mosquitoes in the chamber treated with plain sesame oil after 45 days. They ran this experiment multiple times with the same dramatic results.

In similar experiments in the lab, the scientists also found that females infected with transgenic fungus laid just 26 eggs, only three of which developed into adults, whereas uninfected females laid 139 eggs that resulted in 74 adults.

According to the researchers, it is critically important that new anti-malarial technologies, such as the one tested in this study, are easy for local communities to employ. Black cotton sheets and sesame oil are relatively inexpensive and readily available locally. The practice also does not require people to change their behavior, because the fungus can be applied in conjunction with pesticides that are commonly used today.

"By following EPA and World Health Organization protocols very closely, working with the central and local government to meet their criteria and working with local communities to gain acceptance, we've broken through a barrier," Lovett said. "Our results will have broad implications for any project proposing to scale up new, complex and potentially controversial technologies for malaria eradication."

Next, the international team of scientists hope to test their transgenic fungus in a local village or community. There are many regulatory and social benchmarks to meet before deploying this new method in an open environment such as a village, but the researchers said this study helps make the case for such trials.

The research paper, "Transgenic Metarhizium rapidly kills mosquitoes in a malaria-endemic region of Burkina Faso," Brian Lovett, Etienne Bilgo, Souro Abel Millogo, Abel Kader Ouattarra, Issiaka Sare, Edounou Jacques Gnambani, Roch K. Dabire Abdoulaye Diabate and Raymond J. St. Leger, was published in the journal Science *on May 30, 2019. This work was supported by the National Institutes of Health (Award No RO1-AI106998). The content of this article does not necessarily reflect the views of the organizations.*

https://wb.md/2WfvGrf

New Diabetes Cases in US Fall by 35% After 20-Year Rise

Rates of diagnosed diabetes in the United States may finally be declining but overall numbers remain high, new findings suggest.

Miriam E. Tucker

The analysis of data for an almost 40-year period (1980-2017) from the National Health Interview Survey (NHIS) was published online May 28 in *BMJ Open Diabetes Research and Care* by Stephen R. Benoit, MD, and colleagues from the Division of Diabetes Translation, Centers for Disease Control and Prevention (CDC), Atlanta, Georgia.

After nearly a two-decade increase in both prevalence and incidence of diagnosed diabetes in the United States, the prevalence — the number of people living with diagnosed diabetes — has stabilized for the past 8 years and there has been a decrease in incidence, driven mostly by that seen among non-Hispanic whites. This reduction means new cases declined by 35% from 2008 to 2017, a sign, perhaps, that efforts to stop the nation's diabetes epidemic are working, say the researchers.

However, they caution, "Causes of the plateauing of prevalence and decrease in incidence are unclear and although the trends are encouraging, the overall burden of diabetes remains high and warrants continued intervention and monitoring."

In a press release, Ann Albright, PhD, director of the Division of Diabetes Translation at the CDC, said: "The findings suggest that our work to stem the tide of type 2 diabetes may be working — but we still have a very long way to go."

"We must continue proven interventions and deploy innovative strategies if we're going to see a continued decline in type 2 diabetes among Americans," she urged.

Diabetes Prevalence: Unchanged Since 2009

Benoit and colleagues calculated annual prevalence and incidence of self-reported diagnosed diabetes (types 1 and 2 combined) for adults aged 18-79 years using the annual, nationally representative cross-sectional NHIS data for the 37-year period. Trends in rates by age group, sex, race/ethnicity, and education were assessed using annual percentage change (APC). All values were age-adjusted.

The overall prevalence of diagnosed diabetes didn't significantly change from 1980 to 1990 (3.5 vs 3.4 per 100 adults; $P = .50$). But after that, it rose significantly by about 4.4% per year from 1990 to 2009, peaking at 8.2 per 100 adults ($P < .001$).

Then it plateaued, with an APC of just –0.3% ($P = .53$) through 2017, at 8.0 per 100 adults, representing about 21 million adults in total. Prevalence trends were similar across demographic groups, except for a 1.1% increase in APC from 2005 to 2017 among adults with more than a high school education ($P = .005$).

While those with a high school education or less experienced a similar plateau to the population in general, their overall prevalence of diagnosed diabetes remained approximately double that of people with more than a high school education.

Diabetes Incidence: Dropping Since 2007

The overall incidence of diagnosed diabetes didn't change from 1980 to 1990 (3.6 vs 3.1 per 1000 adults; $P = .97$). After that, it increased significantly, with an annual percentage change of 4.8% ($P < .001$), from 1990 to 2007, peaking at 7.8 per 1000 adults.

Thereafter it began dropping significantly, at an APC of –3.1% ($P < .001$) down to 6.0 per 1000 adults in 2017. This corresponded to a drop from about 1.73 million cases per year of diabetes in 2008 to 1.34 million cases per year in 2017.

Significant trends among subgroups included a decline among non-Hispanic whites in 2008-2017, with an APC of –5.1% ($P = .002$), and an increase among adult Hispanics with more than a high school education in 1999-2017, with an APC of 4.2% ($P = .02$).

What's Behind the Changes?

The specific cause for the large decrease in diabetes incidence can't be determined from these data, Benoit and colleagues note.

Trends in several type 2 diabetes risk factors, including intake of added sugar, sugar sweetened beverages, total calories, and physical inactivity, peaked in the mid-2000s and plateaued or decreased thereafter. However, causal inferences can't be made, they say.

Moreover, they point out, "obesity and severe obesity trends have increased over the past 10 years and prediabetes remains unchanged and high, affecting 84 million US adults, or 34% of the US adult population."

Changes in American Diabetes Association recommendations for the screening and diagnosis of diabetes may have also had an effect, including the lowering of the fasting glucose threshold for diagnosing diabetes in 1997, and the 2010 recommendation for use of HbA_{1c}, a less sensitive indicator than glucose.

"Although an encouraging sign of success, due to the persistence of major risk factors such as obesity and prediabetes, we caution that

trends are likely affected by changing awareness, detection, and diagnostic practices," Benoit and colleague write.

Extended lifespans of people diagnosed with diabetes likely contributed to the lack of reduction in prevalence, they add.

"Even in the event of true reductions in incidence, the high prevalence and declining mortality signifies a continued high overall burden of diabetes," they stress.

"For these reasons, we urge a continued emphasis on multilevel multidisciplinary prevention to reduce both type 2 diabetes and diabetes complications," they conclude.

The authors are all employees of the CDC and had no disclosures.

BMJ Open Diabetes Research and Care. 2019;7:e000657. Full text

http://bit.ly/2Z84KGV

Traditional medicines must be integrated into health care for culturally diverse groups

Traditional Chinese herbal remedies are today used in many countries.

Josephine Agu

View current jobs from University of Technology Sydney

Many people seek complementary treatments for various ailments. Perhaps herbal remedies to cure a cold, or acupuncture to ease lower back pain.

“Complementary medicine” refers to practices outside Western medicine, adopted from other cultures, and often used in high-income countries.

But “traditional medicine” covers a range of practices and therapies indigenous to their practising population. Based on historical and cultural foundations, it operates outside of mainstream health care.

So for example, traditional Chinese medicine is indigenous to the Chinese and is therefore classified as a traditional medicine. But when it’s used by non-Chinese ethnicities, we’d call it a complementary medicine.

While many people use complementary medicines, traditional medicines form a particularly important influence on the way migrants look after their health.

This can present a challenge in the delivery of Western medical care to diverse communities in their destination countries. But even where there’s little consensus around their efficacy, as we strive to achieve better health outcomes for culturally and linguistically diverse people, we must recognise traditional and complementary medicines as an essential component of their health care.

A holistic approach

Traditional and complementary medicines used among culturally and linguistically diverse populations include herbal medicine, acupuncture, massage, traditional Chinese medicine, yoga, ayurveda, homeopathy, and tai chi. Different modalities are favoured in different communities.

Ayurveda is more than 5,000 years old and native to India. It combines lifestyle, diet, exercise and predominantly plant products as treatment options. Translating to “life science”, it aims to cleanse a person of disease-causing substances and restore balance in the body. Ayurvedic practitioners believe this approach is effective in managing a number of acute and chronic conditions including diabetes, cancer, anxiety and rheumatoid arthritis.

While some studies point to its efficacy – one found ayurvedic formulations were comparable to conventional medicines such as glucosamine to treat knee osteoarthritis – varied results and limited study designs make it difficult to draw firm conclusions.

Meanwhile, traditional Chinese medicine has evolved since it was first used more than 2,000 years ago. But it remains grounded in its aim to treat the whole body, rather than targeting the problem alone. Encompassing practices including tai chi, acupuncture, and a variety of herbal remedies, Chinese medicine is today used to prevent and treat many conditions. Patients with knee osteoarthritis

who practised tai chi recorded significant improvements, while there have been positive results for acupuncture in relieving lower back pain and nausea associated with chemotherapy. Traditional Chinese medicine has also been used for the prevention of heart disease and stroke, and to improve quality of life for people with chronic heart failure.

A recent review found certain Chinese medicines may control some risk factors for heart disease, like diabetes and high blood pressure. But several studies were limited by small sample sizes and flawed research designs.

Herbal remedies from Chinese medicine and beyond are employed to treat a range of conditions. St John's wort has been used to treat mild depression, Ginkgo Biloba for memory loss, and ginseng for musculoskeletal conditions.

Despite some promising results, a substantial gap still exists between the strength of evidence supporting many of these practices and consumers' use and acceptance of traditional and complementary medicines.

If the evidence is limited, why should we pay attention?

Some migrant communities experience poorer health than their host populations. For example, the rates of type 2 diabetes are higher among migrants than in the wider Australian population.

It's important to recognise that for minority groups, feeling as though a doctor doesn't understand their cultural needs can be a barrier to help-seeking.

For instance, if a person doesn't believe their doctor will approve of their use of traditional medicines, they may not disclose it. We know non-disclosure of traditional and complementary medicine use is common among culturally diverse groups.

This can be dangerous, as some traditional and complementary medicines can negatively interact with other drugs.

Where patients feel their practitioners are non-judgemental or even accepting of their traditional medicine use, they are more likely to disclose it. So medical providers may benefit from education around different types of traditional and complementary medicines, including culturally sensitive methods to enquire about their use.

Acupuncture, a popular complementary therapy, has its roots in Chinese medicine. From shutterstock.com

What does Australia need to do?

The most mature integrative health care systems are evident in Asia. Countries like South Korea and India have regulated traditional and complementary medicines into their national health policies.

To effectively tackle health inequities, our health systems need to consider and address the impact of cultural influences on patients' health-care decisions. This is vital even when the treatments they value may not be grounded in evidence.

Investigating and considering these practices will ultimately help us to design and facilitate safe, effective, culturally sensitive and coordinated care for all patients and communities across Australia.

Professor Jon Adams contributed to this article.

PhD candidate, University of Technology Sydney

University of Technology Sydney provides funding as a founding partner of The Conversation AU.

http://bit.ly/2Z19n5s

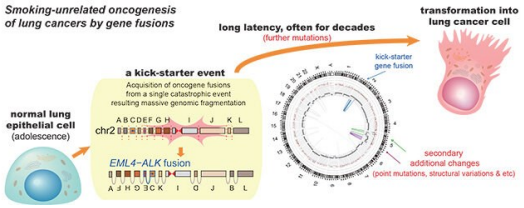
Early genome catastrophes can cause non-smoking lung cancer

Some teenagers harbor catastrophic changes to their genomes that can lead to lung cancer later on in life, even if they never smoke

Catastrophic rearrangements in the genome occurring as early as childhood and adolescence can lead to the development of lung cancer in later years in non-smokers. This finding, published in Cell, helps explain how some non-smoking-related lung cancers develop.

Researchers at KAIST, Seoul National University and their collaborators confirmed that gene fusions in non-smokers mostly occur early on, sometimes as early as childhood or adolescence, and on average about three decades before cancer is diagnosed. The study showed that these mutant lung cells, harboring oncogenic seeds, remain dormant for several decades until a number of further mutations accumulate sufficiently for progression into cancer.

This is the first study to reveal the landscape of genome structural variations in lung adenocarcinoma.



Smoking-unrelated oncogenesis of lung cancers by gene fusions **KAIST**

Lung cancer is the leading cause of cancer-related deaths worldwide, and lung adenocarcinoma is its most common type. Most lung adenocarcinomas are associated with chronic smoking, but about a fourth develop in non-smokers. Precisely what happens in non-smokers for this cancer to develop is not clearly understood.

Researchers analyzed the genomes of 138 lung adenocarcinoma patients, including smokers and non-smokers, with whole-genome sequencing technologies. They explored DNA damage that induced neoplastic transformation.

Lung adenocarcinomas that originated from chronic smoking, referred to as signature 4-high (S4-high) cancers in the study, showed several distinguishing features compared to smoking-unrelated cancers (S4-low).

People in the S4-high group were largely older, men and had more frequent mutations in a cancer-related gene called KRAS. Cancer genomes in the S4-high group were hypermutated with simple mutational classes, such as the substitution, insertion, or deletion of a single base, the building block of DNA.

But the story was very different in the S4-low group. Generally, mutational profiles in this group were much more silent than the S4-high group. However, all cancer-related gene fusions, which are abnormally activated from the merging of two originally separate genes, were exclusively observed in the S4-low group.

The patterns of genomic structural changes underlying gene fusions suggest that about three in four cases of gene fusions emerged from a single cellular crisis causing massive genomic fragmentation and subsequent imprecise repair in normal lung epithelium.

Most strikingly, these major genomic rearrangements, which led to the development of lung adenocarcinoma, are very likely to be acquired decades before cancer diagnosis. The researchers used genomic archaeology techniques to trace the timing of when the catastrophes took place.

Researchers started this study seven years ago when they discovered the expression of the KIF5B-RET gene fusion in lung adenocarcinoma for the first time. Professor Young-Seok Ju, co-lead author from the Graduate School of Medical Science and Engineering at KAIST says, "It is remarkable that oncogenesis can begin by a massive shattering of chromosomes early in life. Our study immediately raises a new question: What induces the mutational catastrophe in our normal lung epithelium."

Professor Young Tae Kim, co-lead author from Seoul National University says, "We hope this work will help us get one step closer to precision medicine for lung cancer patients."

The research team plans to further focus on the molecular mechanisms that stimulate complex rearrangements in the body, through screening the genomic structures of fusion genes in other cancer types.

This study was supported by the National Research Foundation of Korea (NRF), Korea Health Industry Development Institute (KHIDI), Suh Kyungbae Foundation, the College of Medicine Research Foundations at Seoul National University and others.

Jake June-Koo Lee, Seongyeol Park et al., Tracing Oncogene Rearrangements in the Mutational History of Lung Adenocarcinoma Cell *177, June 13 2019, online publication ahead of print at May 30, 2019* https://doi.org/10.1016/j.cell.2019.05.013

http://bit.ly/2HQ8B5r

Wrong side surgical errors substantially underreported and totally preventable

Although rare, may be more common than generally thought

Performing a procedure on the wrong side of a patient's body, although rare, may be more common than generally thought. More than 80 wrong side error (WSE) incidents were reported across 100 hospitals in Spain over the past decade, according to new research being presented at this year's Euroanaesthesia Congress (the annual meeting of the European Society of Anaesthesiology) in Vienna, Austria (1-3 June).

While this might be just the tip of the iceberg, the authors stress the opportunity for improvement. "The stark reality is that due to the lack of reporting to incident databases, these figures most likely represent an underestimate of the true situation", says Dr Daniel Arnal from the Hospital Universitario Fundación Alcorcón, Madrid, Spain who led the research. "However, the reporting of wrong side errors have led to substantial corrective measures to prevent their repetition in our hospitals."

Further prevention of wrong side errors requires the correct implementation of surgical safety checklists (with every team member present), and the creation of a standardised surgical site marking protocol, while increasing reporting of case occurrence and reducing the shame felt by medical teams associated with these events, researchers say.

Although wrong side errors seem preventable, they continue to occur. Previous studies have estimated 1 wrong side surgery per 100,000 procedures and 1.3 wrong-side nerve blocks per 10,000 procedures.

To provide more information on how often and why they occur, and on the safety mechanisms needed to prevent them, Arnal and colleagues analysed WSE incidents reported to SENSAR (Spanish Safety Reporting System in Anaesthesia and Resuscitation), which covers 100 predominantly large hospitals across Spain between 2007 and 2018.

Overall, 81 incidents were reported in 11 years, with high numbers of WSEs noted in orthopaedic (48%) and ophthalmology (28%) surgery.

36 (44%) of these WSEs were related to the surgical procedure, and the surgery was actually performed in half of these cases. The remaining 45 (56%) WSEs involved the anaesthetic technique (the wrong side of the the body given anaesthesia), with an incorrect nerve block performed in 91% of cases. Severe harm was caused on three occasions.

Analysis of WSEs suggests several common causes and systemic failures. In two-thirds of cases, the absence or incorrect use of the surgical checklist was reported. Other factors included rushing and poor communication amongst the medical team.

"Our findings highlight the need for adequate training and appropriate use of surgical check-lists, as well the creation of a standardised surgical site marking protocol, the correct revision of clinical history and imaging tests, and involving patients in their own safety", says Dr Arnal. "While these serious wrong side events are extremely rare, our mission should be to drive them down to zero."

http://bit.ly/2W8wo4L

Nature’s first aid kit: a fungus growing on the side of birch trees

Birch polypore has been used for various health problems. What is the true medical basis behind the anecdotal folklore?

Rowena Hill*

If you've ever stopped to admire a birch tree, you may unknowingly have something in common with a 5,300-year-old mummy called Ötzi. In 1991, hikers found Ötzi in an alpine glacier on the Austrian-Italian border, and perfectly preserved with him were pieces of fungus attached to leather cords, safely stowed in his bag. That fungus is the same one you can see growing on birch trees today: the birch polypore.

Sometimes called birch bracket, and known to scientists as *Fomitopsis betulina*, the polypore is a parasite that slowly kills the birch before feasting on the dead tree until there is nothing left.

The scientists who first identified Ötzi's ancient birch polypore speculated that he could have used it for medical purposes, as some European cultures in more recent human history have been known to do.

With recorded applications ranging from pain relief, wound dressing, antiseptic and even cancer treatment, birch polypore has been used as a broad spectrum therapy for various health problems. But is there a true medical basis behind the anecdotal folklore?

A drug cocktail

Numerous studies have revealed that birch polypore does indeed produce compounds with antibiotic, antifungal, anti-inflammatory, antioxidant, and anticancer properties. Piptamine, polyporenic acids and triterpenoids are all compounds produced as part of the fungus' self-defence mechanism against bacteria, explaining its observed antibiotic value. When tested on dogs and mice suffering from cancer, as well as cancerous cells grown in the lab, birch polypore extracts had a range of anticancer effects such as reducing tumour size and cell growth.

It's hard to identify the mechanisms producing these results, however, as the activity of specific birch polypore compounds is not well understood – they have mostly been studied together in one combined extract, rather than individually isolated. Even more intriguing is that this whole cocktail seems to be more effective than single compounds, which may be a result of a synergistic interaction between the separate ingredients. Further research will be needed to disentangle the relationships in the birch polypore cocktail.

Ultimate eco-plaster

Pharmaceuticals are not the only thing that we can look to birch polypore for, though. All fungi have cells walls predominantly made up of things called polysaccharides. The most abundant of these is chitin, which also gets converted into another polysaccharide called chitosan. Both chitin and chitosan have roles in keeping cells hydrated and help protect from bacteria and other fungi, making them ideal components of wound treatments such as hydrogel, membrane and sponge dressings – with the additional benefit of being biodegradable

Birch polypore can come in many different shapes and sizes, but they almost always grow on birch trees. **Christopher Willans / shutterstock**

Another kind of polysaccharide found in fungal cell walls are D-glucans, which have been shown to help regulate the immune system, as well as having some anticancer and antibiotic activity. A specific type of D-glucan in birch polypore is also able to speed up healing by accelerating the movement of cells to the wound site.

Look to the Fungi for new medicines

While the medical explanation is plausible, we will never categorically know that Ötzi used his birch polypore to treat injuries or ill-health. What we do know, thanks to modern chemical analysis, is that the historical use of birch polypore is grounded in real medical properties.

The State of the World's Fungi report, produced recently by my colleagues at the Royal Botanic Gardens, Kew, highlighted how

important fungi have been for the discovery and production of drugs, but also how little we have explored the vast fungal diversity for such uses: addressing new challenges such as antibiotic resistance could well rely on the potentially over 3m unknown species. Fungi have evolved extraordinary compounds and mechanisms which we can utilise for human health, and traditional practices – as in the case of the birch polypore – can act as a signpost for where to look.

*PhD Researcher, Fungi, at Kew Gardens and, Queen Mary University of London

Queen Mary University of London provides funding as a member of The Conversation UK.

http://bit.ly/2Z3fW7r

Misconduct not mistakes are the chief reason chemistry papers are retracted

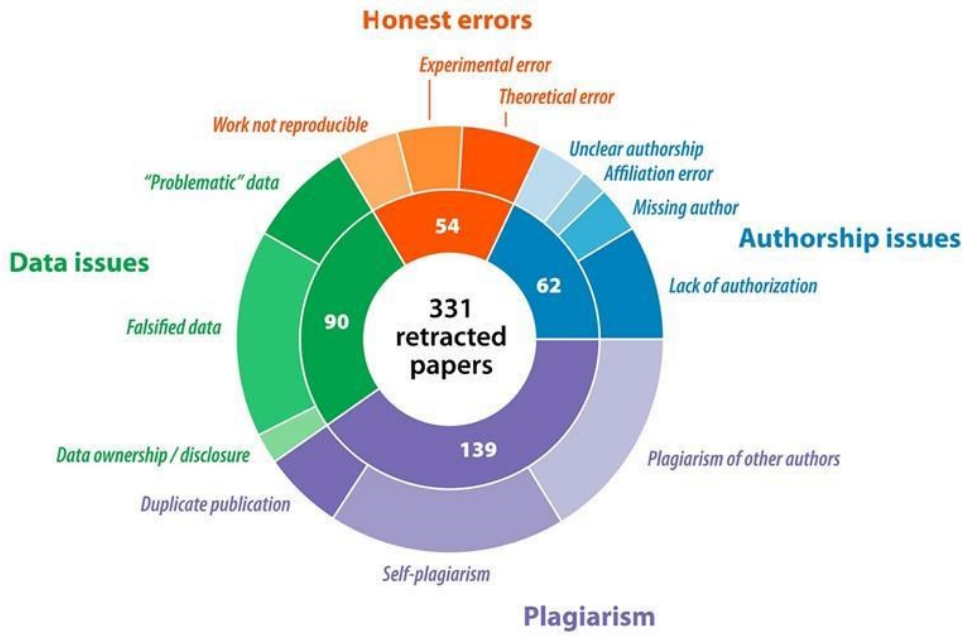
Analysis prompts call for publishers to be more open about the reasons a paper is withdrawn

By Emma Stoye

Most retracted chemistry papers are removed from the literature as a result of academic misconduct, such as plagiarism and falsified data, rather than 'honest mistakes', a study of retractions in 2017 and 2018 has shown.

François-Xavier Coudert, a theoretical chemist at the French National Center for Scientific Research, used Elsevier's Scopus database to identify 331 retracted papers in chemistry or materials science, and analysed the reasons given in the retraction notices. Of these, 139 (42%) cited plagiarism – including duplicate publication and self-plagiarism – and 90 (27%) cited data issues, such as falsified data or data that was vaguely described as 'problematic'.

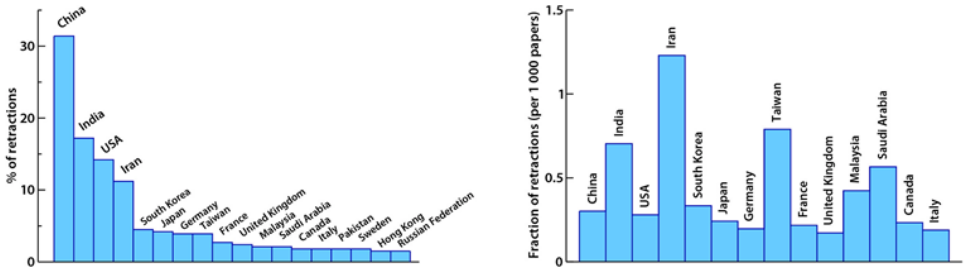
'I've been interested for a bit of time in the practices of publishing and their interaction with misconduct,' says Coudert, who has publicly criticised 'cryptic' retraction notices in the past. 'I really expected there would be more retractions for honest mistakes which, I am sure, happen from time to time in every lab. But it is far from representing the majority of cases.'



Source: © 2019 American Chemical Society

Just 54 (16%) of the retractions in the study were deemed to be due to honest errors – those not attributed to misconduct. These included errors of theory or data analysis, experimental errors and a lack of reproducibility.

Coudert also looked at the geographic distribution of authors on retracted papers, and found that this tended to correlate with chemistry papers in general, although certain countries were overrepresented in retractions, namely India and Iran. 'It's sometimes commonplace to link China to shady publication ethics, in particular due to cash incentives for publication and certain high-profile cases. But at least in the case of chemistry, China does not have a significantly higher retraction rate than the US,' says Coudert.



Distribution of author affiliations per country for retracted papers (left). Retraction rate per country, i.e. number of papers retracted divided by total number of papers published in the country over the same period (right)
***Source:* © 2019 American Chemical Society**

He says the study highlights the need for openness and transparency in the investigations that lead to research being retracted. 'Many retraction notices are quite opaque, and retraction sometimes occur a long time after the issues were raised. We need a more transparent process of investigation when serious concerns are raised.'

Ivan Oransky, co-founder of the blog *Retraction Watch*, agrees. 'It's always great to see someone looking at retractions in a scientific, data-driven way,' he says, adding that studies like this highlight the importance of having a 'fully searchable, comprehensive database of retractions'.

Retraction Watch recently built and launched a database containing more than 19,000 retracted papers that is available to researchers on request. 'Any scholar who contacts us and has a research question, we send them a download of the entire thing,' Oransky says, adding that the number of requests has been increasing since the data became available. 'We hope that more people will study this in future.'

'I also completely agree with [Coudert's] conclusions about the opacity of a lot of these notices,' he adds. 'We've been arguing for better retraction notices since 2010.'

F-X Coudert, Chem. Mater., *2019*, ***31***, *3593 (DOI: 10.1021/acs.chemmater.9b00897)*

http://bit.ly/2QHYWB0

North Korea swine flu outbreak puts South on edge

Seoul is worried a swine flu outbreak in North Korea could cross the heavily militarized border and devastate the South's US$5.9 billion pork industry

South Korean troops stationed along the world's last Cold War frontier have been put on high alert in the face of a new infiltration threat from the nuclear-armed North—fever-stricken wild boar.

An outbreak of African swine fever that has cut swathes through China, Vietnam and Mongolia has spread to the isolated country, sparking worries that sick animals crossing the heavily militarized border could devastate the South's US$5.9 billion pork industry.

"We need to focus on preventing wild boars in the North from entering our territory," the South's Prime Minister Lee Nak-yeon said Saturday after visiting a pig farm near the Demilitarized Zone (DMZ) that divides the two countries.

African swine fever is known to be harmless to humans but is fatal to pigs and wild boar and has devastated supply chains in China—the world's largest consumer of pork—where authorities have ordered the culling of hundreds of thousands of pigs.

Pyongyang told the World Organisation for Animal Health that 77 out of 99 pigs had died from the disease at a farm near the China border, according to Seoul's agricultural ministry.

The ministry said Friday that the disease is "highly likely" to hit the South, and the government has ordered fences to be erected at farms along the border to prevent possible contact between pigs and wild boars.

Seoul believes Pyongyang raises some 2.6 million pigs across 14 state-run farms. The outbreak could worsen food shortages in the impoverished North, where, according to the World Food Programme, its output last year hit the lowest level since 2008.

In the South, there are about 6,700 pig farms across the country, and pig farming accounts for 40 percent of the total livestock industry.

In 2011, a devastating outbreak of foot-and-mouth disease hit the entire Korean peninsula and resulted in the culling of nearly 3.5 million cattle, pigs and other animals in South Korea alone.

While its bristling fortifications, rolls of barbed wire and trigger happy North Korean troops mean crossing the DMZ can be deadly for humans, the zone has been untouched by development and is a haven for wildlife.

Last October a rare Asiatic black bear was photographed in the zone, Seoul's environmental ministry said.

http://bit.ly/2If4kYn

New breast cancer drug found to boost survival rates by 30 percent

New form of drug drastically improves survival rates of pre-menopausal women with the most common type of breast cancer

By Agence France-Presse

A new form of drug drastically improves survival rates of pre-menopausal women with the most common type of breast cancer, researchers said on Saturday, citing the results of an international clinical trial.

The findings, presented at the annual meeting of the American Society of Clinical Oncology in Chicago, showed that the addition of cell-cycle inhibitor ribociclib increased survival rates to 70 percent after three and a half years.

The mortality rate was 29 percent less than when patients were randomly assigned a placebo.

Lead author Sara Hurvitz told AFP the study focused on hormone receptor-positive breast cancer, which accounts for two-thirds of all breast cancer cases among younger women and is generally treated by therapies that block estrogen production.

"You actually can get synergy, or a better response, better cancer kill, by adding one of these cell-cycle inhibitors" on top of the hormone suppression, Hurvitz said.

The drug works by inhibiting the activity of cancer-cell promoting enzymes known as cyclin-dependent 4/6 kinases. The treatment is less toxic than traditional chemotherapy because it more selectively targets cancerous cells, blocking their ability to multiply.

An estimated 268,000 new cases of breast cancer are expected to be diagnosed in women in the US in 2019, while the advanced form of the disease is the leading cause of cancer deaths among women aged 20 to 59.

Growing menace

Though advanced breast cancer is less common among younger women, its incidence grew two percent per year between 1978 and 2008 for women aged 20 to 39, according to a previous study.

The new trial, which looked at more than 670 cases, included only women under the age of 59 who had advanced cancer — stage four — for which they had not received prior hormone-blocking therapy.

"These are patients who tend to be diagnosed later, at a later stage in their disease, because we don't have great screening modalities for young women," said Hurvitz. In addition, patients who develop breast cancer early tend to have more complex cases.

"That's what makes us so excited, because it's a therapy that's affecting so many patients with advanced disease," added Hurvitz.

A pill is administered daily for 21 days followed by seven days off to allow the body time to recover, since two-thirds of patients have a moderate to severe drop in white cell count.

Jamie Bennett, a spokeswoman for Novartis, which markets the drug under the brand name Kisqali and funded the research, said it cost $12,553 for a 28-day dose.

But, she added, "the majority of patients in the US with commercial insurance will pay $0 per month for their Kisqali prescription."

There is no cure for metastatic breast cancer and the majority of the women on the drug will require some form of therapy for the rest of their lives.

‘Significant survival benefit’

Oncologist Harold Burstein, who was not involved in the research, said it was “an important study,” having established that the use of cyclin inhibitors “translates into a significant survival benefit for women.”

Burstein is with the Dana-Farber Cancer Institute in Boston.

“Hopefully, these data will enable access for this product for more women around the world, particularly in healthcare systems which assess value rigorously as part of their decisions for national access to drugs,” Burstein added.

Moving forward, Hurvitz said she was interested in investigating whether ribociclib could help nip cancer in the bud at an earlier stage.

“We want to go and look at those women diagnosed with early stage disease, small tumors, tumors that haven’t gone to the lymph nodes or haven’t gone to other parts of the body and see if we can stop it from returning later from metastasizing,” she said.

A new global clinical trial is now underway.

http://bit.ly/2JWkbyi

Blood transfusion during liver cancer surgery linked with higher risk of cancer recurrence and death

Receiving blood transfusion during surgery for common type of liver cancer associated with much higher risk of cancer recurrence and dying prematurely

Receiving a blood transfusion during curative surgery for the most common type of liver cancer (hepatocellular carcinoma) is associated with a much higher risk of cancer recurrence and dying prematurely, according to new research being presented at this year's Euroanaesthesia congress (the annual meeting of the European Society of Anaesthesiology) in Vienna, Austria (1-3 June).

The risk was markedly increased even when only a small amount of blood was transfused, researchers say. Findings showed that transfusion of 1 to 4 units of blood increased the risk of cancer recurrence by 23% and death by 55% compared to matched controls.

"Our findings from a large cohort highlighted a significant association between red blood cell transfusions and the risk of cancer recurrence as well as a dose-response relationship between the amount of transfusions and death after curative surgery for liver cancer", says Dr Ying-Hsuan Tai from Taipei Medical University Shuang Ho Hospital in Taiwan who led the research.

"The reason why blood transfusions substantially worsen cancer prognosis remains unclear, but it is likely to be related to the suppressive effects on the immune system."

Hepatocellular carcinoma (HCC) is the fifth most common form of cancer worldwide and the third most common cause of cancer-related deaths. It occurs frequently in people with cirrhosis (scarring of the liver) due to previous damage from hepatitis B or C virus, or long-term alcohol abuse.

Surgery to remove the cancer and a margin of healthy tissue that surrounds it (resection) is a curative treatment for people with early-stage liver cancers who have normal liver function. Whilst advances in liver surgery have reduced operative blood loss considerably, liver resection still carries the risk of excessive blood loss and need for blood transfusion.

The extent to which blood transfusion worsens cancer outcomes after surgery is poorly understood. For several decades, research has reported conflicting findings, and has been unable to conclude whether blood transfusion itself is causing problems, or if other

factors such as the underlying medical conditions that make surgery necessary might be to blame.

In this study, Tai and colleagues investigated the effect of perioperative blood transfusion on cancer prognosis following HCC resection in 1,469 patients without lymph node involvement or metastasis undergoing surgery at Taipei Veterans General Hospital, Taipei, Taiwan between 2005 and 2016. Researchers assessed postoperative disease-free survival and overall survival up to September 2018. Using statistical modelling (a technique called inverse probability of treatment weighting) they were able to match patients who had equivalent age and health conditions when comparing their outcomes.

Almost 1 in 3 patients (30%; 447 patients) received 1 to 4 units of allogeneic (from another individual) blood during or within 7 days of surgery, whilst more than 1 in 10 (12%; 179 patients) were given more than 4 units.

During a median 45 month follow-up, analyses showed that cancer was 23% more likely to recur in patients who received a transfusion (1-4 units) compared to those not given a transfusion, whilst those who received more than 4 units faced a 18% greater risk of recurrence compared with those who received none.*

Compared to those not given a transfusion, patients given 1-4 units of blood were 55% more likely to die from any cause, whilst those receiving 4 or more units had almost double the risk of death.

The authors conclude: "These data highlight the need for randomised trials to evaluate the influence of transfusion on cancer outcome and identify the level of anaemia that patients undergoing liver cancer surgery can withstand (or the minimum amount of blood they need to have transfused) with minimal adverse effects in order to guide practice. Until these trials have been completed, surgeons should use practices that reduce the risk of bleeding and the need for transfusion."

http://bit.ly/2wBpdaF

Chest cavity fire during emergency cardiac surgery

Unique case of a man who suffered a flash fire in his chest cavity during emergency heart surgery

At this year's Euroanaesthesia Congress (the annual meeting of the European Society of Anaesthesiology) in Vienna, Austria (1-3 June), doctors present the unique case of a man who suffered a flash fire in his chest cavity during emergency heart surgery caused by supplemental oxygen leaking from a ruptured lung.

Dr Ruth Shaylor and colleagues from Austin Health in Melbourne, Australia, where the incident took place, warn that the case highlights the potential dangers of dry surgical packs in the oxygen-enrich environment of the operating theatre where electrocautery devices (using heat to stop vessels from bleeding) are used.

In August 2018, a 60-year-old man presented for emergency repair of an ascending aortic dissection--a tear in the inner layer of the aorta wall in the chest. The patient had a history of chronic obstructive pulmonary disease (COPD) and had undergone coronary artery bypass grafting one year previously.

As surgeons began to operate, they noted that the man's right lung was stuck to the overlying sternum with areas of overinflated and destroyed lung (bullae; often caused by COPD). Despite careful dissection, one of these bullae was punctured causing a substantial air leak. To prevent respiratory distress, the flows of anaesthetic gases were increased to 10 litres per minute and the proportion of oxygen to 100%.

Soon after, a spark from the electrocautery device ignited a dry surgical pack. The fire was immediately extinguished without any injury to the patient. The rest of the operation proceeded uneventfully and the repair was a success.

"While there are only a few documented cases of chest cavity fires--three involving thoracic surgery and three involving coronary

bypass grafting--all have involved the presence of dry surgical packs, electrocautery, increased inspired oxygen concentrations, and patients with COPD or pre-existing lung disease", explains Dr Shaylor.

"This case highlights the continued need for fire training and prevention strategies and quick intervention to prevent injury whenever electrocautery is used in oxygen-enriched environments. In particular surgeons and anaesthetists need to be aware that fires can occur in the chest cavity if a lung is damaged or there is an air leak for any reason, and that patients with COPD are at increased risk."